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CARCINOMA OF THE ORAL CAVITY*

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Many branches in the domain of the specialties of medicine and surgery share the interest in the subject of carcinoma of the oral cavity; the surgeon, the dentist, the laryngologist, the internist and the general practitioner, in addition to the dermatologist, manifest keen interest in it. It is possibly a case of too many cooks spoiling the broth, for the subject lacks the uniformity of opinion in important details which is absolutely imperative, if any appreciable amount of therapeutic good is to be accomplished.

This title covers carcinoma as it affects the following locations: the lip, the tongue, the cheeks, the floor of the mouth, gingiva and the palate.

Quick,[1] whose contribution to the subject has been most noteworthy, stated that the question of diagnosis is so apparent in most cases, that unless a loose piece of tissue can be easily removed for biopsy, one should not remove a specimen for diagnosis, as the lymphatic channels might be opened and dissemination of the lesion encouraged.

In general, there are two types of carcinomas[2] affecting the oral cavity, the superficial papillary type and the deeply infiltrating type.

The superficial papillary type presents an ulcer of varying size, frequently covered by a crust which drops off and reforms periodically. The base of the ulcer is covered by neoplastic nodules and shows but little infiltration. Later, this may become the second type.

The deeply infiltrating type shows a relatively small area of surface ulceration at first. The ulcer is deep in its infiltration, with raised indurated edges, and may be crateriform, with central sloughing. The growth progresses by invasion of the deeper structures and the surface ulceration gives no indication of the extent of the disease.

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* Read before the Section on Dermatology and Syphilology at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 12, 1929.

1. Quick, D.: Radium in the Treatment of Epithelioma of the Lip, J. Radiol. 2:1, 1921.

2. Ewing, James: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928, pp. 885 to 894; Quick (footnote 1).

The question of differential diagnosis lies in the exclusion of syphilis [3] in its primary and tertiary stages; tuberculosis, nodular or ulcerative; simple ulcers; fissures; warty growths; new growths other than carcinoma, and granulomas.

As the reaction of the mucous membrane is singularly alike in syphilis, tuberculosis and early carcinoma, no hard and fast rules can be laid down for differential diagnosis, except for the invariable characteristic hardness of carcinoma, its usually single character, its foundation on a preexisting defect of the mucous membrane, all of which calls for the clinical experience of a dermatologist, who is more familiar with the recognition of these criteria than any other specialist.

Hasty conclusions in the differentiation between syphilis and carcinoma, unmindfulness of their frequent coexistence, energetic treatment for syphilis in the presence of a carcinoma, will lead to disaster by the stimulation of the proliferation of the epithelial cell and rapid extension of the carcinomatous process.

Carcinoma of the skin develops most frequently on the site of a preexisting dermatologic defect such as a nevus, scar, tuberculosis, keratosis, etc, Although little has been said on this subject, with the exception of leukoplakia,[4] a similar condition exists in the mucous membrane. The development of carcinoma occurs on seborrhoic dermatitis areas of glossitis (chronic), ulcerations about the gingiva and they frequently escape the attention of physicians. It is in this connection, however, that the greatest amount of preventive work can be accomplished.

Innumerable [5] examples have been used to show that chronic irritation plays a definite rôle in the production of carcinoma, but irritants pointed out were mostly of mechanical or physical nature. In carcinoma of the mouth one is impressed with the fact that, almost uniformly, the patients have a septic mouth, and that defects of the mucous membrane in the presence of microbic irritation, coming from pyorrhea alveolaris in its various stages, seem to be the criteria for the production of carcinoma of the mucous membrane.

Arthur Hopewell Smith [6] put it as "physiologic resistance reduced through infection about alveolar process."

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3. Blair, V. P., and Ivy, R. H.: Essentials of Oral Surgery, St. Louis, C. V. Mosby Company, 1925, p. 295.

4. Ewing (footnote 2, first reference, p. 885).

5. Essential Facts About Cancer, American Society for the Control of Cancer, January, 1924, p. 33.

6. Smith, Arthur Hopewell: The Normal and Pathological Histology of the Mouth, Philadelphia, P. Blakiston's Sons & Company, 1928, vol. 2, p. 269.

Duncan Fitzwilliams [7] stated: "My dentist once asked me if I had ever seen cancer of the tongue in an edentulous person. The thought had never occurred to me before and I had to confess I could not recall a single case. Many had been sent to have their teeth seen to as soon as they were examined and since then I have noted bad teeth in almost every case. Probably nowhere in the body are the tissues subject to the influence of sepsis so continually as in the mouth of the poorer classes of patients."

Moorehead and Dewey [8] quoted Bashford, who believed "that carcinoma biologically is a function incident to the decay of tissues."

Ewing [9] said: "Among preventable cancers the most obvious is the intra-oral group. Cancer of the lip, tongue and tonsil are due to bad teeth, tobacco and syphilis in the order named. Broken, decayed and projecting teeth continually tear the adjacent mucosa. Pyorrhea often adds an affective irritant. Buccal uncleanliness is of great importance."

Dobson [10] emphasized the importance of lack of dental cleanliness as a contributory factor in carcinoma of the mouth.

Schempp,[11] considered dental caries, smoking and leukoplakia as predisposing causes.

Much has been said of ill-fitting dentures, pressure sores caused by them as a factor in the causation of carcinoma. My experience has been entirely different. During the last three years I have had the opportunity to examine edentulous patients in the office of a prothodontist. Some of the patients came in with nasty looking deep ulcers from the pressure of ill-fitting dentures, some of such ulcers lasted over an extended period of time. So far I have not seen a single one of these cases becoming carcinomatous if the patient has been edentulous for a period of one year or over. It should be remembered that roots may be present. If there is any doubt, roentgen examination of the mouth is advised.

This brings one to the consideration of the examination of the mouth. For the examination of the mucous membranes, no better technic can be adopted than the one described by Stokes.[12] Particular attention must be paid to the gingiva, congestion and discoloration; sponginess or presence of pus must be carefully noted. After this type of inspection,

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7. Fitzwilliams, Duncan C. L.: The Tongue and Its Diseases, New York, Oxford University Press, 1927, p. 371.

8. Moorehead, F. B., and Dewey, K. W.: Pathology of the Mouth, Philadelphia, W. B. Saunders Company, 1925, p. 389.

9. Ewing, James: Cancer Control, Surgical Publishing Company of Chicago, 1927, p. 167.

10. Dobson: Cancer Rev. **4**:21, 1929.

11. Schempp, E.: Cancer Rev. **1**:398, 1926.

12. Stokes, John H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1926, pp. 55 to 60.

transillumination of gums for shadows disclosing deeper infection, roentgen examination of the teeth and their alveolar sockets, and lastly, vitality tests of the teeth are carried out.

The résumé of the four precedures gives one a clinical picture which can be intelligently coordinated.

They are not only of academic interest, but they also form an important part of the treatment when this is prescribed.

Twenty-four consecutive patients presenting carcinoma of the oral cavity were studied for this presentation. Their ages varied from 34 to 73 years; the duration of the disease was from four to thirty-six months. All showed evidences of gross oral sepsis as proved by one or more of the following observations:

(*a*) Hyperemic, bleeding, spongy gums, from most of which pus could be expressed easily; (*b*) discolored, tartar-covered, uneven, ragged-edged, jagged, worn-down, sharp or broken teeth, showing absorption about the alveolar processes and the presence of pus pockets; (*c*) lacerations about the mucous membrane of gums, cheeks and tongue, and (*d*) fetor oris.

Treatment for carcinoma of the oral cavity should be considered in the light of what has been said before about the existing microbic irritation. I consider of the greatest importance the thorough cleaning out of the mouth as the first procedure. A serious condition like carcinoma, which so frequently terminates in the death of the patient, demands no half-hearted methods in its handling. If there is a chance for the patient at all, it lies in the fact that energetic and systematic treatment is instituted with a definite therapy in mind. It is much better and safer for the patient for one to overdo in this respect than for one to conserve tissues to the detriment of the patient.

The mouth should be cleaned before treatment is attempted, for as Quick [13] said, "infection alters the natural course of the disease and interferes with the normal reaction to radium quite as much as it does with operative measures."

Extraction of all the teeth is usually necessary because in such patients, one cannot delay the treatment by waiting until the mouth is cleaned up in any other way. Just as soon as possible, usually within ten days, the primary site of the carcinoma and glandular metastases, if any are present, are attended to, either with radium emanations, gold filtered, or with electrocautery.

As an example, in a case of carcinoma of the gingiva, the following steps are considered routine:

1. Discontinuance of the use of tobacco.
2. Extraction of all the teeth.
3. A waiting period of about ten days, until the mouth gets into condition for treatment.

4. Implantation of radium emanation, gold filtered, 1 millicurie each, 1 cm. from the border of the lesion at 1 cm. distance from each other, encircling the lesion, then implanting the mass itself so as to implant 1 millicurie of radium emanation to each cubic centimeter of tumor.

5. Under local anesthesia, exposure of the lymphatic glands and implantation of gold in glands visible in the same ratio as those in the mouth.[13]

6. Deep roentgen therapy to the cervical glands in case the glands are not palpable and after the reaction from radium subsides. The dose is 200 kilovolts, 4 milliamperes; the filler, 0.5 copper and 2 mm. aluminum; the distance, 50 cm. and the size of the aperture, 16 by 16 cm. This treatment is given for thirty minutes, twice a month for six months unless an erythema appears, in which case the roentgen therapy is discontinued.

7. Examination of the patient every three months thereafter for a period of five years.

Instead of the radium implantation, wide excision with electrocautery may be practiced, but the so much quoted V-shaped excision seems to be incorrect, as properly stated by Quick [14] who maintains that the real situation is an inverted V as far as the tumor mass is concerned.

The routine described can be adapted to all patients with the necessary modification, due to the location of the lesion.

I might have been going far afield from what is considered as domain in dermatology, especially from the standpoint of treatment. It is not my intention to ask any one to follow such procedures, but it is my earnest desire to have the problem coordinated and supervised by the dermatologist. He should intelligently prescribe the steps and have them carried out with precision. Surely the frequent recurrences of the disease, its unsurgical treatment, the ignoring of dental infections, the carrying out of surgical measures or the implantation of radium in the presence of infection need a new type of supervision of the field.

SUMMARY

Carcinoma of the oral cavity is associated with a septic mouth in most patients. Its treatment should not begin until the sepsis has been removed.

In the prevention of carcinoma, not only mucous membrane defects but the condition of teeth should be investigated.

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ABSTRACT OF DISCUSSION

DR. KINGERY, Portland, Ore.: Dr. Hollander has emphasized three points which are always worthy of consideration. First, the importance of careful examination of the mucous membrane whenever it is in the slightest degree indicated. If one approaches the examination with certain facts in mind, fewer lesions will

13. Quick, D.: Carcinoma of the Lower Jaw, Am. J. Surg. **1**:360, 1926.

14. Quick, D.: Radium in Adequate Dosage in the Treatment of Carcinoma, J. A. M. A. **89**:2035 (Dec. 10) 1927.

be overlooked. Briefly, the possibilities of differential diagnosis must include the group of conditions of a simple inflammatory nature, transitory in character and superficial in depth of involvement; the group of chronic granulomatoses that are inflammatory, but with a tendency to deeper involvement, definite destruction and scar tissue formation; finally, the group of degenerative changes, characterized by fixation, destructive tendencies and functional impairment. Each condition presents its own clinical picture and this picture is more readily recognized if the underlying histologic changes are constantly in mind. Second, the manner in which lesions may respond to therapy. A relatively malignant-appearing lesion may melt away under treatment, and subsequent observation may reveal no tendency to recur. Another lesion relatively benign clinically may withstand all therapeutic attack and steadily progress to a fatal termination. There is suggested, therefore, an inherent biologic difference in cell type which, in turn, might well be influenced by the factors of oral sepsis discussed by the essayist. Finally, in the matter of etiology, irritation ranks high, and the mechanical type, the chemical type and the bacterial type are to be considered. Unquestionably, in the latter type there is no reason why pyorrhea alveolaris cannot play a part. Whether this is in the nature of continuing an irritation of long standing, or whether the continued presence of such a process impairs the tissues' ability to respond to treatment cannot be definitely said. At any rate, I think it is worth while to use the treatment Dr. Hollander has suggested, with the hope that it will improve the prognosis now necessary in such cases.

Dr. Cole, Cleveland: Dr. Hollander made a point which should be emphasized, and that is the influence of old snags in the mouth in connection with malignancy in this area. I make it a routine to insist on the removal of all such snags before any treatment is instituted, and I have seen instances in which the process would go down 50 per cent within one week after the irritating snag is removed. This an excellent point.

Dr. Grindon, St. Louis: While I am quite certain of the effect of local conditions, such as pyorrhea, I would say that infectious septic processes, not only in the mouth but elsewhere may affect the development of cancer in other parts of the body. Dr. Burrows, formerly of St. Louis but now of Pasadena, has shown that cancer situated anywhere in the body is favorably influenced by the removal of septic conditions, whether in the mouth, the cervix, or elsewhere.

Dr. Percy, Los Angeles: I am particularly interested in what Dr. Hollander does with teeth that are surrounded by the malignant process. To extract them, as dentists are often wont to do, is, I am convinced, a dangerous procedure, not only because it stimulates and disseminates the malignancy, but because not infrequently a meningitis follows. Before removing such teeth, I sterilize them and the surrounding tissues thoroughly by playing an acetylene gas flame from a torch, such as jewellers employ in welding watch springs, etc. I apply the flame until the teeth become brittle and flaky. A temperature of this degree destroys not only the pyogenic infection that surrounds them but also penetrates their sockets and kills the cancer cells within. When the teeth are thus removed as a preliminary, the involved lip can be taken away with the cautery under the same anesthetic. If the leather-like surface, remaining after the disease is removed, can be kept dry, that is, protected from the saliva for at least two weeks, the lip will frequently be practically reproduced, vermilion border and all. This cap protects the normal repair cells in the redevelopment of the lip. Human saliva seems to interfere with the reproduction of normal tissue cells. In such an event, the usual excess of connective tissue and loss of substance will result, but never to the deforming degree that follows the customary V-shaped excision that is made with the cold

knife. There is, therefore, finally less of the "sucker mouth" type of result in evidence. In my experience, dentists make an earlier diagnosis of carcinoma in and about the mouth than do physicians. This is undoubtedly due to the more comprehensive instruction in dental schools on the early signs of oral malignancy. If the patient has a positive Wassermann reaction in a case that is clinically carcinoma, he is most unfortunate if given either mercury or the arsenical compounds. Bismuth and, possibly, the iodides have a much less stimulating effect on the growth of cancer. If there are no palpable glands in the neck at the time of the cautery removal of the lip I do not disturb either side unless the patient is of a mental type that cannot be trusted to report immediately for their removal should glands subsequently appear. My reason for this is that metastasis above the clavicle develops very late, in the larger number of patients.

DR. TAUSSIG, San Francisco: I agree with Dr. Hollander that carcinoma of the oral cavity is a dermatologic problem, and that its treatment should be directed by the dermatologist. I cannot, however, agree with Dr. Hollander that sepsis in the mouth is a prime factor in the causation of carcinoma. It is probably one factor, and it is agreed that an infected mouth should be cleaned up, but I think removing a whole set of teeth is rather a radical procedure. Frequently other antiseptic measures will serve. One point has interested me for a long time, and that is the removal of a small section of tissue to establish the diagnosis. I believe that if there is any doubt of the diagnosis, a biopsy should be done.

DR. HOLLANDER, Pittsburgh: I regret that my presentation was not as clear as I would like to have had it, but I overran my time and did not have a chance to speak on several important phases. I wanted, principally, to emphasize that it is not necessary for the dermatologist to carry out the treatment that I presented, but this supervision would be of much benefit. One should approach the patient with a definite therapy in mind, having prepared the patient to receive the greatest benefit from the treatment. This our colleagues in surgery have apparently not done in the past. Operations in the presence of sepsis are usually avoided by the surgeons in the ordinary run of cases. Operations on the tongue or oral mucous membrane are frequently carried out in the presence of sepsis as I have shown you in my paper. As to the actual treatment, it does not make much difference whether one uses a blow-torch, cautery or any other procedure with the same result in mind, as long as the area of sepsis is removed before the second part of the therapy is undertaken. Local anesthesia usually suffices for most of the procedures advocated. No hard and fast rules can be made regarding the removal of the cervical glands. As long as no palpable glands are present I think one should not attempt any block dissection, for I consider that the lymph glands are one of the factors of safety which lie between the patient and his grave. Should the glands be palpable, they can be exposed under local anesthesia and treated with emanations of radium in the same manner as the primary lesion is treated. I reiterate that block dissection, in which the glands are not involved, might be detrimental to the patient.

HEMATOGENOUS INFECTIOUS DISEASES OF THE SKIN *

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Twenty-five years ago, I wrote an essay on hematogenous infections and toxic dermatoses. In this paper, I critically summed up the existing knowledge in the light of my own experience. Today I shall again attempt such a summary, but only as far as it is possible to do so in a lecture; that is, only on general lines, and almost entirely restricting myself to infectious processes, to newer facts and to experiences in my own clinic.

At the time of my first paper, I defined hematogenous dermatoses as "Those diseases in which the agent causing the disease is brought, by the blood, directly into the skin and there causes its corresponding manifestations." I should not yet care to change anything in this definition.

I defined as toxic those dermatoses in which substances in solution affect the skin, without it being demonstrable that these substances are deposited there (conditions produced by autotoxic drugs or other substances).

I separated from these conditions those in which elements which were not in solution (tumor cells, and also nonorganic substances such as bismuth) reached the skin or in which substances originally in solution were there deposited in corpuscular form; that is, endogenous, such as icterus, or exogenous, such as argyria. This separation still seems to me justified—colloidal chemistry will probably here also be able to bridge seeming gaps—but I here leave all these questions aside. Unchanged and clear is the definition of the last group, the infectious dermatoses; that is, those in which the pathogenic living organisms reach the skin through the blood route and which E. Fränkel wished to call "metastatic dermatoses."

Knowledge of the acute hematogenous processes that accompany generalized diseases (I do not here include measles, scarlet fever, etc.) has been greatly increased. Much more is known about the exanthems caused by staphylococci, streptococci, meningococci, pneumococci and by pneumonia, pyocyaneus, typhoid and paratyphoid bacilli. E. Fränkel, particularly, worked a great deal in this field. It has been learned that

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the different microbes cause very different types of skin eruptions, due as well to the differences in their point of attack in the skin as to their different effects. It has also been learned, however, that the exanthems caused by the same microbe can vary widely on account of individual differences of reaction or even through different localizations on the body. To these numerous generalized infections must be added the polymorphous exanthems of gonorrhea (even excepting the so-called keratotic type which is of uncertain pathogenesis) and the apparently exceptionally rare nodular (erythema nodosum-like) eruptions in ulcus molle and in lymphogranuloma inguinale. The hematogenous skin diseases in tuberculosis, syphilis, leprosy and mycoses are of particular importance in this specialty.

In tuberculosis the so-called classic types are separated from the tuberculids, and there is that third group which is now probably best designated by the term (relatively) anergic. Besides the certainly hematogenous acute and subacute miliary tuberculosis and the bacillary forms of pityriasis rubra Hebrae, and besides the leg ulcers which can develop from acute erythema nodosum-like nodules, other forms are known. These are multiple cold abscesses (tuberculosis colliquativa) which are found not alone in children but also in adults. They can often persist for a long time in the pure form, and especially without any combination with lupous lesions; that is, they show a peculiar characteristic reaction. This is not due only to an affinity for the subcutaneous tissues, for in these cases the cutaneous processes also develop in the characteristic manner. The views concerning the pathogenesis of tuberculosis luposa are still widely divergent. It must be particularly stressed that the preexistence of tuberculosis of the lung is not necessarily proof that the skin lesions are of endogenous origin. For tuberculosis of the lung is too frequent, and it may be due to its presence that a superinfection from the outside or per contigutatem takes on a lupous character on account of the existing skin allergy. The postexanthematous cases are often characterized by their large number of lesions, by their symmetry and by their relatively benign course. There is no doubt that isolated single lesions of lupus can also originate hematogenously, but it is difficult to demonstrate this pathogenesis with certainty. In contrast to the lupous form, verrucous tuberculosis is generally proved to be ectogenous in most cases; it is probably also due to superinfection. In rare cases it may also be hematogenous in origin.

The bacillary hematogenous mode of origin is now almost generally accepted in the case of tuberculids in the stricter sense (particularly papulonecrotic, lichenoid and nodular forms). Only a short time ago, however, on the basis of my own observations, I called attention to the occurrence of tuberculids of a single extremity in combination with a

deep tuberculosis of the hand or foot; in these cases a lymphogenous origin, although not yet proved, must still be seriously considered. Lesions in the vicinity of lupus are, in exceptional cases, similar to lichen scrofulosus or acnitis; these surely originate by the lymph route.

The anergic group contains sarcoids and lupus pernio, lupus miliaris and perhaps also granuloma annulare. All these forms are either entirely or almost entirely hematogenous; particularly in the two first named is this definitely shown by the existence of histologically analogous lesions in the lungs, in the bones, in the lymph glands, etc.

In syphilis, after the demonstration of spirochetes in all the secondary lesions, one could no longer doubt their infectious origin. It is beyond doubt that the first roseolas ensue soon after the hematogenous transport of spirochetes to the skin; in all later lesions one is, in principle, permitted to be undecided whether they are due to a renewed dissemination or whether they are attributable to microbes which have remained and again achieve a pathogenic effect owing to changes in the state of allergy or changes in their own growth. It can be considered as probable that both these possibilities occur—what their relative frequency may be is undecided. There are, on the one hand, the recurrences in healed primary lesions, and on the other hand, spirochetes in the blood in secondary syphilis, even ectogenous auto-infections can be considered (contact [abklatsch] papules); entirely analogous considerations are true in tertiary syphilis.

In leprosy the hematogenous localizations dominate almost the entire picture. It is well known that they sometimes develop insidiously and sometimes suddenly in the form of acute exacerbations, the so-called "reactions" (akute Schübe). Bacilli have been found more and more frequently in the blood, particularly during the reactions. The hematogenous dissemination here plays an important rôle not only for the diseases of the skin but also for some of the nervous and visceral lesions.

I shall skip the less thoroughly studied infections in which the microbes are carried by the blood stream, such as malleus, anthrax and yaws.

Besides the already mentioned pyemias, lichen pyodermicus must be mentioned. This condition was described in E. Hoffmann's clinic but until now has not been followed further. I have no personal experience with this disease. On the other hand, a more accurate understanding has been gained in the field of the hematogenous origin of dermatomycoses. Here the main representations are the long well known infections with trichophyton and favus, and also those with microsporon and epidermophyton.

The first of these forms was that which I originally called lichen trichophyticus, and which, following the suggestion of Bloch, I later

named lichenoid trichophytid. The different forms of "mykids" are well known. That they are hematogenous infections in the great majority of cases can scarcely be doubted, as Saeves and many other authors have caused hematogenous trichophytic lesions by intracardial injections in animals and as Max Jessner and Ambrosoli and others have demonstrated fungi in the circulating blood in human beings. In spite of this, as I have repeatedly emphasized, ectogenous and lymphogenous infections probably occasionally cause analogous lesions, even though these do not generally lead to the same pictures.

It is natural that trichophytids should generally, though not exclusively, occur in the deep forms of trichophyton infections, for these present the two principal conditions for their occurrence—the opportunity for the fungi to enter the blood vessels and the formation of an allergy. In other words, trichophytids, like tuberculids, generally are infections of the skin modified by a certain form or degree of allergy.

In human beings one hardly ever sees hematogenous trichophytic skin lesions containing fungi such as those which can be produced in animals at will. However, in sporotrichosis and related conditions typical abscesses containing fungi are the rule. The "sporotrichids" that have been observed until now seem to be caused by auto-inoculation. In my clinic at Breslau, Beatrice Kesten, of New York, succeeded in producing hematogenous mykid-like nodules in rats. One must here think also of blastomycosis, which in the known "systemic" cases can produce hematogenous skin lesions. But even very superficial pustular blastomycotic eruptions sometimes give the absolute impression of a hematogenous dissemination (superficially, Mrs. Kloptock's case in a newborn infant).

Having here reviewed, only in the very roughest lines, of course, the hematogenous infections of the skin, I should now like to speak of a few of the cardinal points in their general pathology. I should like to be briefest on the question of why in certain diseases or in certain cases invasion of the blood sometimes occurs, and why the invaders sometimes do and sometimes do not become pathogenic for the skin. How small the lesions may be through which even such bulky microbes as the skin fungi can penetrate and enter the blood has been shown by the experiments of Kogoj and Werner Jadassohn, etc. Besides this it is known, for instance, through the histology of primary lesions of syphilis, that microbes enter the open blood vessels. Thus the differences in the structure of the pathologic processes (granulation, necrosis, organization of thrombi, etc.) can determine the frequency of blood infection. These pathologic processes are themselves dependent on the type and development of the reaction, which differs according to both the individual and the kind of microbe. In this there are as factors on the one hand influ-

ences that mobilize the microbes and favor their deposit in the skin—such as traumas, active and passive hyperemias and inflammations in the skin—and on the other hand, sensitizations and influences that weaken the resistance of the organism as a whole; sometimes both types of factors are combined, as for instance in measles. Everything that displaces the proportion of skin to microbes in the direction favoring the latter is here of importance. All this is more or less obvious, but, in the nature of things, also vague. In principle, one must count with the infectious hematogenous dermatoses those exanthems in which, as already mentioned in the case of syphilitic roseolas, the microbes are dispatched to the skin and remain there, lying dormant until the allergy is formed, increased or even supplied artificially, and then only cause a reaction; e. g., lichen scrofulosus provoked by tuberculin.

One can be somewhat more exact concerning the question of why in infections with both ectogenous and hematogenous lesions these two forms either are identical in appearance or differ. On viewing this entire field one finds that all possible variations are here represented, from the more or less complete identity of both kinds of lesions (as in lupus, for instance,) and the cases with marked differences (for instance, primary lesions and secondary papules) to differences which seem to be almost qualitative (primary and tertiary syphilitic lesions, tuberculosis and tuberculids, trichophytic infections and trichophytids). If one looks more closely one sees that here also all forms of passage occur; as a matter of fact they are found as well in the various diseases as in the individual cases of the same disease. This is because, while all possible changes in macro-organisms and micro-organisms influence the form of the disease, the importance of these factors still is apparently dominated by that of the allergy. The allergy develops in the different diseases and in different cases in such a tremendous number of varying ways that it has been said that "allergy can explain everything."

This sounds like a criticism. It is obvious, however that that faculty of the organism through which it changes its reaction form as a response to the influences of a microbe must be just as dependent on the patient, and on the specific qualities of the irritant as is the case in all other reactions and irritations.

Now it is obvious that in principle one must consider an allergic influence only as emanating from the primary skin lesion in those diseases in which such lesions and hematogenous distributions are known. We test the presence of this allergy with products of the microbes in the well known way (tuberculin, etc.). Only a short time ago, however, I pointed out that this manner of testing is often crude, and that one must therefore be careful not to conclude from the

negative result that there is a lack of allergy. It is probably recalled that one formerly considered tuberculids and roseolas, and later also trichophytids, as toxic manifestations.

Many years ago, I as well as Darier and many others, attempted to explain the peculiarities of the tuberculids by a weakening or even a destruction of the bacilli in the blood, and I tried to explain the syphilids by a modification of the macro-organism. E. Fränkel expressed his belief that the microbes arriving with the blood may not come into such intimate contact with the skin tissues and that they therefore have a milder action. This, however, does not hold true in either syphilids or the hematogenous trichophytic diseases in animals. In one case or another, however, all these factors may have some importance. Thus, M. Jessner and H. Hoffmann demonstrated a special effect of the serum of allergic persons on trichophyton fungi, and also showed that fungi coming from the skin lesions differ in their cultures from those derived from the glands or the blood of the same patient. Martenstein and Mrs. Granzow found that the serums of patients with different forms of tuberculosis varied in their effects on tubercle bacilli. All these factors, however, are probably less important for the hematogenous lesions than is the skin allergy; it is this which determines the proportion between microbes and tissue structures.

Many years ago Unna said that in typhoid the roseola is the grave of the bacilli. Today one would have to say that the allergy kills or eliminates the microbes, because the allergic skin reacts even to the small amount of endotoxin produced by the microbes that die in the living tissue as well as in the culture. In such sites the endotoxins may continue to act for some time; one must suppose this to be the case, for example, in tuberculids and in some trichophytids. Here also is seen the variability of the process based on the individual differences of the patient and on the specificity of the microbes. After measles there can be seen in one case a hematogenous lupous, verrucous or colliquative tuberculosis, and in another case a lichenoid form. The modifications due to the allergy make the microbes numerous in secondary syphilids and few in tuberculids. And the grade of changed reaction, which is designated as specific anergy, contributes to the form of the lesions of the sarcoid group in tuberculosis. Syphilids are rich in spirochetes when the luetin allergy is lacking, and poor when it is present.

A further question of general pathology which is important for the understanding of hematogenous infections is that of the point of attack of the microbes in the skin. L. Philippson, who is probably the first to have attacked this question, said that those lesions which he called embolic are localized mainly in the veins of the subcutis. He

proved this by anatomic studies in hematogenous tuberculosis. At that time I had called attention to the fact that the great majority of hematogenous infections do not originate in the subcutis, but in the cutis and particularly in the papillary body.

According to E. Fränkel, in his examinations of acute exanthems the smaller arteries of the cutis and subcutis are principally those which are most markedly harmed by the bacteria which enter them, and which in some cases multiply vigorously (this is also true in tuberculosis miliaris). Emboli of cocci are localized almost exclusively in the capillary arteries, sometimes even in the vasa vasorum of the small arterial tributaries. They can also penetrate the lymph vessels of the papillae (E. Fränkel).

It is beyound doubt, for both clinical and anatomic reasons, that the localization in the blood vessels of the skin is not constant in the hematogenous infectious dermatoses. Determining points of view for judging the different deposits are, in the first place, purely physical: the conditions of flow, the size of the vessels and the dimensions of the microbes. In these, individual differences play a great rôle. One need only remember the importance of peripheral cyanosis and of varicose veins in certain exanthems. Next, biochemical factors can be of importance, and in various ways. In the first place, different parts of the blood vessel system can have different affinities for various microbes; here also, individual factors can be of importance. This is shown, for instance, by the repeated or sole preference of certain rare syphilids for occurrence in a particular patient. Next, it depends on what conditions of transport the various microbes meet with in the blood vessels. Just as in the blood elsewhere, so they can be destroyed in the vessels of the skin; here the products arising in their destruction (the endotoxins) can lead to sterile reactions. Either true bacterial emboli or single bacteria growing into such colonies can, without destroying or breaking through the vessels, cause sterile reactions in the vicinity. Or the microbes can arrive in the skin, either with or without destroying the vessel walls, and there give rise to their characteristic processes. Besides all these possibilities, there also exist the hematogenous effects on the skin which are caused by endotoxins or ectotoxins which microbes produce in distant organs.

If the hematogenous skin infections are considered from these points of view, one comes to the following result: These exanthems are localized in either (1) the papillary body, and in the general cutis without connection with the glands, (2) the hair and follicular apparatus or (3) the subcutis. In the papillae the capillary loops particularly favor the deposit of microbes. The inflammatory processes which originate at this point can naturally proceed into the cutis, so that the papillary

origin can no longer be observed. The same probably holds true for some lesions originating in the cutis and growing into the papillae; in the cutis also the points at which the branching vessels leave the thicker venous and arterial nets are particularly disposed for the deposit of microbes. Clinically, this whole group is represented by the most frequent forms of hematogenous exanthems: roseolas, papules, vesicles and pustules.

A special rôle is undoubtedly played by the follicles. Both the network of vessels that is wound about the hair and the sebaceous gland, and the small ascending and descending branches in the papilla of the hair show a mechanical disposition for the deposit of microbes. But here another factor must probably be included. For it is surely not purely chance that in tuberculids and trichophytids the follicular localizations are so frequent, and that in just these hematogenous exanthems one must attribute a particular importance to the allergic state, and also that in the analogous syphilids peculiar allergic conditions are at play, as is shown both by their occasional local sensitiveness to tuberculin and by their tuberculoid structure. Only a short time ago I showed by an example that the follicular apparatus seems to have certain special immune biologic peculiarities, for in ectogenous superficial trichophytic infection the fungi can remain in the follicles, and there be pathogenic for a certain period after the superficial epithelium is healed, free from fungi and (temporarily) immune. Particularly in the lichenoid trichophytids one shall perhaps have to think of the fact that the fungi which are deposited in the follicular vessels are relatively very near to the horny substance; they can therefore reach their favorite medium after but a short passage through the living cutis, in which they find it difficult to thrive. The predilection of bromine and iodine for the follicles shows that these latter possess certain general biochemical peculiarities entirely aside from their immune biologic qualities. It is remarkable that few analogous conditions of the sweat glands are known (e. g., rare cases of plane lichenoid tuberculids).

In the third group mentioned, that of the deep nodules, the veins are often of particular importance. This is shown not only by the original histologic examinations of Philippson, and by further histologic observations, but also by the fact that not infrequently the nodules are accompanied by cordlike thickenings which apparently represent the veins. The great importance which Darier attributes to the veins in the case of gummas also speaks in this direction. In this I naturally do not mean that such deep nodules cannot also originate in arteries and capillaries, as has been seen in tuberculids (Schidachi, Stein). But the usual depositing in the veins is astonishing, for this does not correspond to the mechanism which one considers as taking place in

embolic processes. Philippson assumed that the microbes remain in the veins on account of the slower flow of blood, after they have been brought through the capillaries by the speedier current. The idea that I, among others, developed in conjunction with Markuse in my first paper, in relation to considerations on the pathogenesis of tuberculids and thrombophlebitis, still seems to me more probable; namely, that the disease of the veins originates in their vasa vasorum. In the latter the circulatory conditions are decidedly similar to those in the papillae or in the vessels of the follicles. Schaumann succeeded in supporting this assumption histologically in a case of subcutaneous sarcoid, a disease which certainly belongs to this group. Perhaps the vasculatory conditions of the valves of the veins may be of importance here. Besides these movements, emboli in the capillaries, with the growth from here into the veins, other factors may play a rôle.

The marked preference of such nodules for localization on the legs must naturally have some connection with the circulatory conditions here.

It must be also particularly stressed that the same microbes which cause the nodules on the legs much oftener cause superficial or follicular lesions on the skin of the other parts of the body (even in the same patient and at the same time). It need not be emphasized that these facts concerning the subcutaneous lesions apply to all nodular tuberculids and syphilids, lepra lesions, pyogenic, gonorrheal and rarely trichophytic nodules, the erythema nodosum in lymphogranuloma inguinale, etc.

I should not like to leave this field without having called attention to a certain fact. As is well known, skin changes (generally pigmentary ones) which are due to external causes, and especially to heat, are not the only ones which adhere in their configuration to the network of the so-called livedo calorica reticularis; for inflammatory processes which are doubtless of endogenous origin can take some branching reticular form which is close to that of the livedo. These forms correspond with livedo inflammatoria racemosa of Ehrmann. Particularly syphilitic and tuberculous processes have been observed to take these shapes (by Adamson, particularly at the junctions of the network [livedo lenticularis] and by Lehner and Kennedy, Urbach, Perutz and Kaiser). I myself know of such "figured" lichenoid tuberculids and tertiary syphilids. In one case, I saw a recurring (perhaps tardive) roseola combined with a livedo racemosa. Many hypotheses exist concerning the anatomic and physiologic bases of livedo reticulata, but probably no certain explanation (compare with Lewis). But the changes in the arteries in livedo racemosa have been repeatedly pointed out, particularly by Ehrmann and his pupils. There is a remarkable

analogy, which it would pay one to study further, in that the embolic bismuth exanthem, as described by Freudenthal, has an entirely similar reticulated and rootlike distribution. In this case the arterial embolic origin is proved; accordingly, one can think of such a pathogenesis in infectious processes showing the same form. At any rate, the reticulated form of hematogenous infections cannot be denied.

Just as the point of attack of the infecting microbes in the different layers and organs of the skin requires further exhaustive study, so also is this required in the problem of the reasons for the different localizations of the hematogenous infectious dermatoses. In this I shall leave entirely out of consideration the reason why the microbes in the blood prefer to settle in the skin, or why they settle only in the skin in one case and do not do so in another—in other words, that which is called the different degrees of dermatropism. I should rather only point out how little is known of the causes of the tremendously varying and often characteristic localizations on the skin. Neither the knowledge of the distribution of the vessels nor that of the structure of the skin can give one a sufficient understanding of the well known predilections of localization. Moreover, these can differ greatly from individual to individual. The predilections of tuberculids for sites with passive hyperemia, of certain exanthems for palmae and plantae, and so on, are examples of predisposing circulatory and anatomic factors. From experience in toxic fixed exanthems and in refractory zones, and from experiments with external irritations, it is known that regions that are seemingly identical anatomically can behave very differently.

There is a somewhat further advance in the knowledge of these phenomena of localization which, for a long time, have been attributed to provocations. Kreibich would like to classify these also under the sensitizations, while I consider the latter to be a more purely biochemical processes. The classic example of provocation in infections was, until recently, syphilis. It has been recognized in this disease that single as well as repeated traumas (in the widest sense of the word, that is, including chemical and actinic effects) can often favor the localization and even the production of a skin lesion. Recently these clinical observations have been successfully imitated experimentally. Even before Inga Saeves, in my clinic in Bern, produced hematogenous trichophytic lesions through intracardial infections, the fact had been strikingly shown that shaved areas seemed to be the preferred localizations. But only when Kogoj systematically continued these observations in my Breslau clinic was it possible actually to force the hematogenous trichophyton lesions in guinea-pigs to selected regions. This could be done through traumas, through inflammatory irritation and through localized cyanosis. The fungi in the blood could be

demonstrated after intracardial and also after cutaneous inoculation. This could be done soon after inoculation (Werner Jadassohn) and also after a certain period following the infection (Sulzberger). It is interesting that the hematogenous trichophytic lesions often appeared exclusively in regions previously influenced. It is reasonably certain that through further experiments of this type more will be learned concerning the mechanisms of hematogenous skin infections and of provocations. From experiments that have remained relatively unconsidered, it can be concluded that other pathologic agents can act in a way similar to that of the fungi. This is shown by the experiments of Calmette, Prowacek and Yamamoto who injected vaccine into the blood and made observations analogous to those mentioned. How differently the various microbes may act in such experiments also is shown by the fact that Biberstein could not obtain skin lesions through intracardial superinfection and local provocation of syphilitic rabbits while Werner Jadassohn demonstrated bacilli in the skin after provocation in tuberculosis of rabbits (not yet published).

It would be tempting to mention the relationships between hematogenous infections and toxic dermatoses. Here there is almost the same range of forms: from the purely erythematous to the nodular (potassium iodide) and hemorrhagic—from the pustular to the granulomatous tumor-like forms (halogens). Only urticaria, the prototype of toxicodermas, is missing among the infections (perhaps not always—E. Fränkel).

In toxicodermas one also meets the riddle of localizations. One can easily understand these analogies, now that at least a great many toxicodermas, especially those caused internally, are being attributed with more and more certainty to antigen—antibody reactions.

In toxic hematogenous dermatoses, sensitizations and desensitizations are as important as allergy in the infectious ones. In the former, one can also contrast a primary effect from the outside and a resorptive one from within (for example, in the case of mercury). The fixed exanthems and also the refractory zones here point to analogous and no less illustrative phenomena than those found in infections. The experiments of Frei and of Sulzberger on arsphenamine dermatitis in animals may open the field for a more exact experimental study of drug eruptions.

Finally, the consideration of the surely infectious and the surely toxic hematogenous dermatoses gives a view of the pathogenesis of the diseases of the skin concerning whose causes nothing certain is yet known. In these one is less able to decide whether they are hematogenous or ectogenous, infectious or toxic, the more the similarities between all these groups have become apparent. Still, some exam-

ples show that, based on the knowledge of the pathogenesis and of the importance of allergic and anaphylactic phenomena, respectively, the questions can be formulated more precisely. I mention only the corymbiform lesions in psoriasis and lichen planus, which form another argument of probability for their infectious nature, and the fact that through knowledge of trichophytids the hematogenous allergic nature of pityriasis rosea has become more probable. It is now understood much better that erythema exudativum multiforme and erythema nodosum are themselves probably caused by microbes, but that their doubles, that is, very similar forms, are toxicodermas. Then, too, the well known phenomenon of Koebner in psoriasis, the "isormorph irritation affect" ("isormorpher Reizeffect" [Kreibich]) becomes more explicable through the experiments in provocation.

Deductions of analogy are dangerous in pathology. However, if one finds facts which agree on a general pathologic basis, and if one builds hypotheses on these, it has been proved by examples that these hypotheses have a great heuristic value; from this standpoint, contemplation of the present knowledge of hematogenous infectious dermatoses, even though aphoristic, seemed to me to be of some interest.

ABSTRACT OF DISCUSSION

DR. PUSEY, Chicago: It is not necessary for me to undertake to emphasize to you the interest of Professor Jadassohn's paper. Professor Jadassohn, however, gave me the opportunity to read his paper and I thus have a better comprehension of the wealth of knowledge of dermatology which it covers and of the philosophic spirit with which he has considered his material. I cannot but express my regret that for your sake he did not feel that he could read his paper in its entirety. I look forward to the time when we may publish it and all may read it in full. I read it with care, with interest and with profit. I can offer no criticism of his statement of clinical facts or his interpretation of them. Indeed I do not feel competent to do this. In saying this I am not assuming any modesty, for I know no one in America or abroad who is entitled to speak on this subject with the authority of Professor Jadassohn. In his paper he gives a summary of the clinical facts that he brings forward and then he passes on to a philosophic dissertation on them. It is an exhilarating experience. I do not know which I admire more, his breadth of knowledge or his philosophic spirit. A day or two ago, in a discussion, Professor Jadassohn warned me that imagination is all right if it is properly controlled by knowledge. This paper is a beautiful illustration of that sort of combination, a brilliant imagination carefully controlled by knowledge.

American dermatology, Professor Jadassohn, is honored by your presence among us, and I shall assume for this section which represents American dermatology, the privilege of saluting you as the doyen of our specialty.

DR. WEIDMAN, Philadelphia: I rise mainly because I do not wish Professor Jadassohn's presentation to pass without additional expressions from this body; he is entitled to them. He has given us another of the learned discussions which we have enjoyed in the literature and in person here in the United States; and today he has demonstrated courage and originality in essaying that blank wall

which we have hitherto labeled as idiosyncrasy where we could go no further in outlining the pathogenesis of a dermatosis. He has suggested the parts that heat, congestion, allergy, inflammation and so forth play in the formations and problems we are only too familiar with in dermatology. Not many years have passed since I was only a pathologist, knowing nothing of dermatology, and one of the first things that worried me when I essayed dermatopathology was the number of discrepancies between the cause of disease and morbid anatomy which are so much more obvious to the dermatologist than to any other specialist. To relate but one, I was particularly baffled by the annular configuration. Why annular? In the internal organs (on serous surfaces) these are excessively rare; indeed, I know of no such thing as a genuinely annular lesion. Perhaps the closest approach is the infarct as viewed on its base. If you look on the outside of the spleen you find a circular lesion—pale in the center, and margined by the trite "zone of collateral hyperemia"—and I attempted to link the pathogenesis here with the annular lesions in the skin. But in the skin the arteries are not "terminal" and we cannot have such a thing as a gross, true infarct. Yet I think there may be at least some such effect in producing annular lesions in the hematogenous infectious dermatoses—at least to the extent of producing a greater or lesser degree of vitiation of the tissues—short of necrosis, which makes it possible for this or that embolus to colonize in this familiar annular configuration. I have enjoyed much this presentation of Professor Jadassohn's.

PROF. JADASSOHN, Breslau, Germany: I only wish to express my many thanks and my regret that I was obliged to be so brief. I hope the paper can be published in full, and then I believe that Dr. Weidman will see that we go quite in the same direction, perhaps in different ways. My tendency is always to try to explain what we see by general pathology.

THE DISTRIBUTION AND EXCRETION OF MERCURY *

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AND

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Mercury and its salts rank among the most widely used drugs in medicine. The therapeutic value of mercury is well established, but certain of the pharmacologic and biochemical aspects of the compounds of this metal have not been thoroughly studied, owing to the difficulty of determining mercury in the presence of organic matter or halogens. Lomholt and Christiansen [1] reported a test which they claimed to be accurate and satisfactory, but it is time-consuming and requires a microbalance. Booth, Schreiber and Zwick [2] reported a test which is accurate, but which has certain limitations mentioned by the authors, such as: it is time-consuming, is inaccurate in the presence of iodides and requires special equipment and technic not common to a clinical laboratory. Young and Taylor [3] recently described a method for mercury determination which is less laborious, is accurate and does not require special technic. By the use of this method the authors, as the present paper reports, have been able to study the rate of excretion of various mercury compounds, their penetration into the cerebrospinal fluid and the effect of acids and alkalis on the rate of excretion in man. In experimental animals, we studied the distribution of the mercury in the tissues during and following the period of active excretion.

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* Read before the Section on Dermatology and Syphilology at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 11, 1929.

1. Lomholt, S., and Christiansen, A.: Metode til bestemmelse af smaa maengder kvaezsolviorganisk substans, Biochem. Ztschr., 1913, vol. 10; quoted by Lomholt, S.: Absorption and Elimination of Mercury in the Different Methods Used in the Treatment of Syphilis, Brit. J. Dermat. & Syph. **32**:353 (Dec.) 1920.

2. Booth, N.; Schreiber, N., and Zwick, K.: The Determination of Traces of Mercury: II. The Quantitative Determination of Mercury in the Presence of Organic Matter, J. Am. Chem. Soc. **48**:1815, 1926. Schreiber, N.; Sollmann, T., and Booth, H.: The Determination of Traces of Mercury: III. The Quantitative Determination of Mercury in Urine and Feces and the Influence of Medication, J. Am. Chem. Soc. **50**:1620, 1928.

3. Young, A. G., and Taylor, F. H. L.: An Electrolytic Method for the Determination of Small Amounts of Mercury, J. Biol. Chem., **84**:377, 1929.

METHOD

Therapeutic doses of the compounds to be studied were administered to patients who were on a controlled diet with known fluid intake. Continuous twenty-four hour specimens of urine and feces were collected and analyzed daily. Spinal punctures were made at varying intervals, and the cerebrospinal fluid was analyzed for mercury. Blood was drawn at the time of lumbar puncture and allowed to clot. This was centrifugated, and the mercury in the serum was determined.

In studying the effect of diet on the elimination of mercury, the patients were started on a diet low in calcium. This diet was then varied to a high calcium neutral, or a low calcium diet plus ammonium chloride. The diets were calculated according to Sherman's tables.[4] The diets, which were high in calcium and low in acid precursors, were used to produce an alkaline condition in the body. In some instances this effect was augmented by the use of calcium lactate. Conversely, a diet low in calcium and high in acid precursors was used to reduce the alkaline condition in the body. This was augmented in some instances by the administration of ammonium chloride. In studying the effect of sodium thiosulphate on the rate of elimination of mercury, the excreta were analyzed for two or three days to determine the normal rate of elimination before the sodium thiosulphate was given. It was then injected intravenously in daily doses of 25 cc. of a saturated solution. In two patients a single therapeutic dose of 10 mg. of mercury as the tetraiodide was administered, and samples were collected until, on analysis, no mercury was found. A second dose of the mercury compound was then given plus daily injections of sodium thiosulphate, and the total amount of mercury excreted for each period was compared.

Rabbits were used for the study of the distribution and storage of mercury in the tissues. The animals were given single intramuscular injections of the compounds to be studied. One half of the group, consisting of seven animals, was killed during the period of active urinary excretion, and the remaining animals were killed after the urine became negative for mercury. The tissues were then analyzed, and the results compared.

COMPOUNDS STUDIED

Potassium mercuric tetraiodide, yellow mercurous iodide, U. S. P., mercuric succinimide and mercuric salicylate were studied. The two former compounds represent inorganic mercury in the water-soluble and water-insoluble states, respectively, as compared to the latter compounds which represent mercury combined with an organic radicle in the water-soluble and water-insoluble states. The study of these substances was made with the hope of determining whether the solubility or chemical constitution of a compound influences the rate of excretion or the penetration into the cerebrospinal fluid. All of the substances were injected intramuscularly, with the exception of the protiodide, which was given by mouth.

Most of the patients studied were suffering from tertiary syphilis. In each instance care was taken to ascertain that there were no demon-

4. Sherman, H.: Chemistry of Food and Nutrition, ed. 2, New York, The Macmillan Company, 1925, p. 421.

strable lesions of the kidneys or other conditions that might influence the urinary excretion.

RESULTS

Yellow Mercurous Iodide Administered by Mouth.—Three patients were studied. Chart 1 shows the rate of excretion of mercury in the urine of two patients for four periods. In each instance, the excretion of mercury was slightly increased when the patient was taking a low calcium acid diet. It is also interesting to note that the curve for the excretion reaches its maximum on the fourth day of each period and then falls to a lower level.

Potassium Mercuric Tetraiodide Administered Intramuscularly.—Four patients were studied. Chart 2 shows the daily rate of elimination

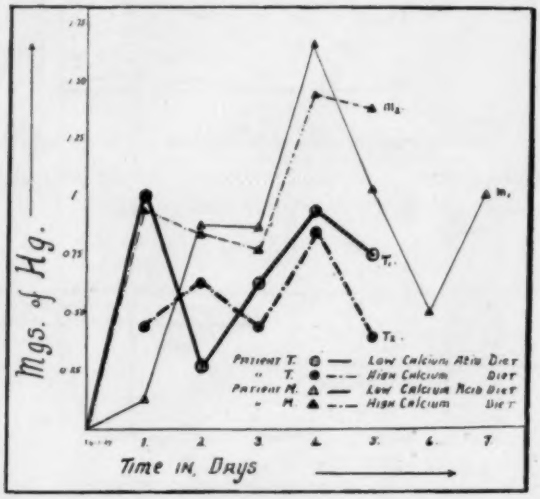

Chart 1.—Urinary excretion of mercury. Yellow mercurous iodide given by mouth; ⅙ grain daily.

of mercury in the urine and stools following a single injection of 1 cc. of solution equal to 10 mg. of mercury in one patient on an ordinary well balanced diet. The data for the other three patients were similar. The highest level of mercury excreted in the urine occurred on the fourth day. The mercury content of the feces is always low as compared to the content of the urine. Chart 3 shows the effect of ingestion of alkali and acid diets on the rate of elimination of mercury in one patient. It will be noted that while the patient was on a high calcium, alkaline diet, the excretion was essentially nil for the first four days, after which there was a small amount of mercury present in the urine. When the patient was given a low calcium acid diet plus ammonium chloride (6 Gm. daily) there was a pronounced increase in

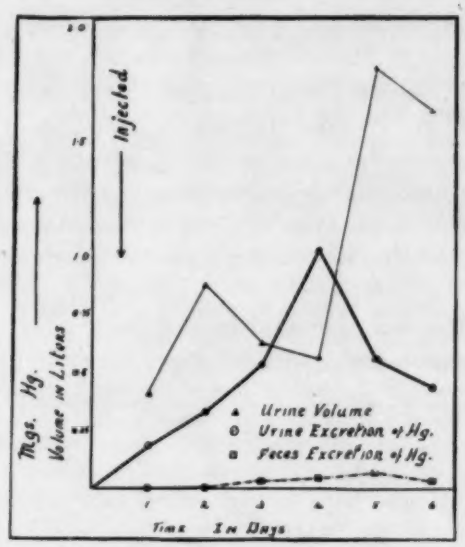

Chart 2.—Curves after the administration of 30 mg. of mercury (intramuscularly) as potassium mercuric tetraiodide (patient Bu.).

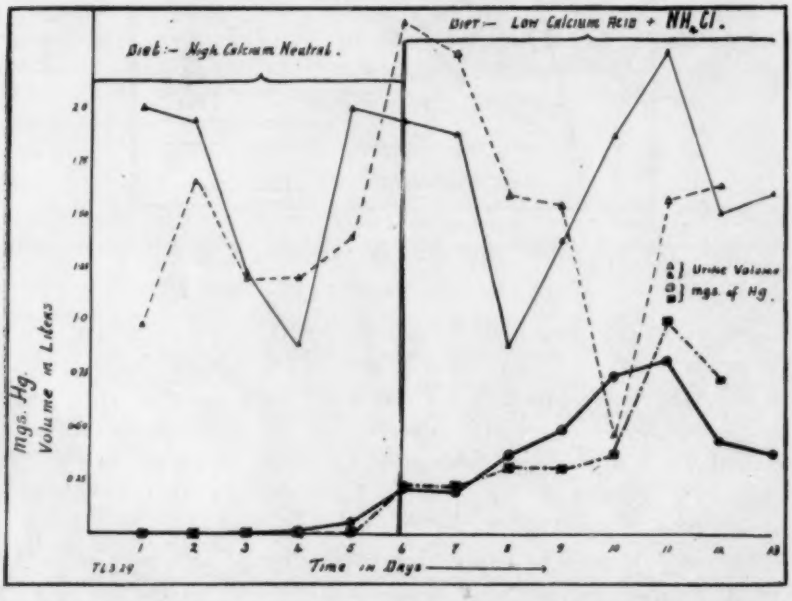

Chart 3.—Effect of diet on the urinary excretion of mercury; 10 mg. of mercury administered intramuscularly as potassium mercuric iodide. The solid curve represents the first period; the broken curve, the second period.

the urinary mercury. The data given in chart 3 are presented in duplicate, as the observations were repeated on the same patient one month apart. Chart 4 shows the excretion of mercury in the feces of the same patient. It is noteworthy that the greatest percentage of increase following the low calcium acid diet and the administration of 6 Gm. daily of ammonium chloride occurred in the feces rather than in the urine. Thus the urinary output was increased three and one-half times as compared to the fecal output, which was increased ten times. Chart 5 shows the effect of administering daily oral doses of 6 Gm. of calcium lactate. It also illustrates that it was possible to stop the excretion of mercury entirely for two days, but that this was followed by active excretion. However, for the six day period that the patient was given

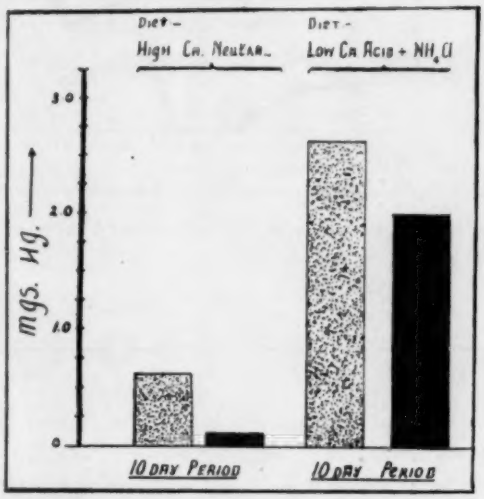

Chart 4.—Comparison of fecal and urinary excretion of mercury with change of diet. The shaded columns represent the amount of mercury in the urine; the solid columns, that in the feces; 10 mg. of mercury administered intramuscularly as potassium mercuric tetraiodide.

calcium lactate, the total excretion of mercury was about half as great as during the control period.

Mercuric Salicylate Administered Intramuscularly.—Three patients were studied. Chart 6 shows the rate of urinary excretion of mercury of one patient when 1 cc. of mercuric salicylate, equal to 37 mg. of mercury, was given intramuscularly. Comparable results were obtained in the other two patients. The curve for excretion does not reach its maximum within the first four days, as occurred when yellow mercurous iodide and tetraiodide were administered. However, the greatest rate of excretion of mercury as a result of the administration of the salicylate occurred between the sixth and the ninth day following the injection.

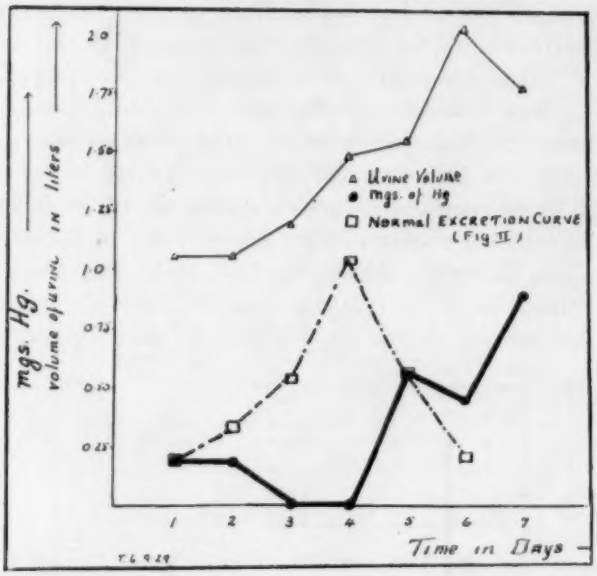

Chart 5.—Effect of calcium lactate on the urinary excretion of mercury.

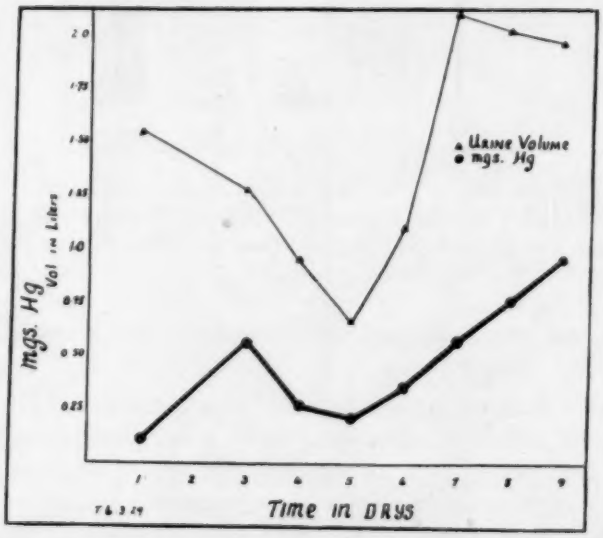

Chart 6.—Urinary excretion of mercury after the administration of salicylate of mercury.

Mercuric Succinimide Administered Intramuscularly.—Six patients were studied. When the patient is given from 1 to 5 ampules containing 1 cc. of mercuric succinimide, equal to 6 mg. of mercury per cubic centimeter, the rate of excretion of this compound is practically the same as that of the tetraiodide. The rate of penetration into the spinal fluid is illustrated in chart 7, which shows the amount of mercury per cubic centimeter of spinal fluid when 20 mg. of mercury was the total unit dose. This chart shows that the concentration in the spinal fluid increases in proportion to the duration of treatment when the mercuric succinimide is administered daily. The saturation point for the cerebrospinal fluid was not determined.

The accompanying table shows the concentration of mercury in the urine and spinal fluid on the fourth day after a single injection of mercury in the form of salicylate, succinimide and tetraiodide. This table shows that it is not possible to predict the concentration of mercury

Penetration of Mercury into the Cerebrospinal Fluid on the Fourth Day Following a Single Intramuscular Injection

Compound	Dose in Mg. of Mercury	Total Mg. of Mercury in Urine on Fourth Day	Total Volume of Urine in Cc.	Micromilligrams of Mercury per Cubic Centimeter of Cerebrospinal Fluid
Mercury succinimide	30	0.350	1,650	0.0
Mercuric salicylate	37	0.300	1,700	3.0
Potassium mercuric tetraiodide	30	1.080	550	2.1

in the spinal fluid from the amount of mercury in the urine. From a comparison of the results in the table with those given in chart 7 it would appear that the penetration into the spinal fluid is greater following repeated small doses of mercuric succinimide than following one large dose; whereas a single dose of mercuric salicylate shows the same concentration of mercury in the spinal fluid at the end of four days as when an equal amount of the succinimide is given in divided doses. The tetraiodide occupies an intermediate position.

Examination of all of the data presented shows that the rate of elimination of mercury is not influenced by the urinary volume.

Effect of Sodium Thiosulphate on Elimination of Mercury.—Four patients were studied. Since the work of Ravaut [5] and Dennie and McBride [6] on the effect of sodium thiosulphate on patients suffering

5. Ravaut, P.: L'importance des traitements internes en dermatologie: L'emploi du cacodylate de soude à hautes doses et de l'hyposulfite de soude, Presse méd. **28**:73, 1920.

6. Dennie, C. C., and McBride, W. L.: Treatment of Arsphenamine Dermatitis, Mercurial Poisoning and Lead Intoxication, J. A. M. A. **83**:2082 (Dec. 27) 1924.

from arsenic poisoning, this substance has been used widely as an antidote for arsenic, mercury, bismuth and other metallic intoxications.[7] Therefore, it was decided to study its effect on the rate of elimination of mercury. Chart 8 shows the results of administering daily doses of 25 cc. of a saturated solution intravenously to a patient suffering from mercury poisoning induced by an overdose of mild mercurial ointment.

It will be noted that a slight change in the excretion of mercury followed the use of sodium thiosulphate. Further work showed that it somewhat decreased the rate of elimination of potassium mercuric tetraiodide given in therapeutic dosage. The same results were obtained when it was administered to patients undergoing mercurial medication with other compounds. No attempt was made to study its effect on experimental animals.

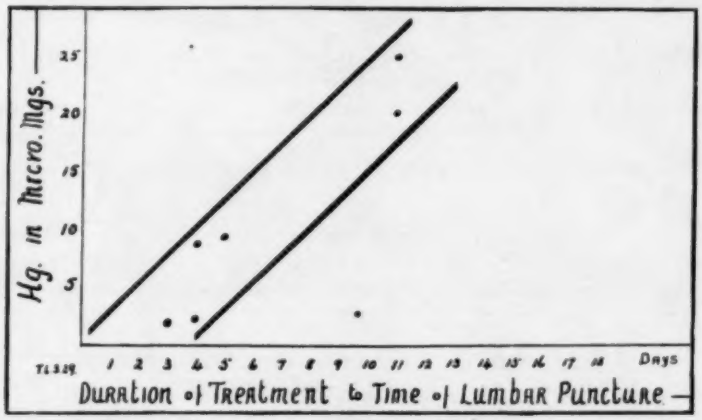

Chart 7.—Penetration of mercury succinimide into the spinal fluid. Standard unit, 20 mg.

Distribution and Storage of Mercury in the Tissues.—Fourteen rabbits were used. Chart 9 shows the distribution of mercury in the tissues during the period of its active urinary excretion as compared with the period after the excretion of mercury in the urine had stopped. Examination of this chart shows that during the period of active urinary excretion the mercury is found in rather high concentration in the muscles, bone, liver and kidney, but that following this period the

7. Hoffmann, E., and Schreus, H. T.: Natriumthiosulfat als Heilmittel für Salvarsan (und Hg.-) Dermatitis, München. med. Wchnschr. **70**:1481, 1923. Sutton, I. C.: The Use of Sodium Thiosulphate in the Treatment of Postarsphenamine Dermatitis Exfoliativa: Report of a Case, Am. J. Syph. **7**:608, 1923. Deussing, R.: Zur Behandlung der Salvarsanvergiftungenmit Natriumthiosulfat, Deutsche med. Wchnschr. **51**:1824, 1925.

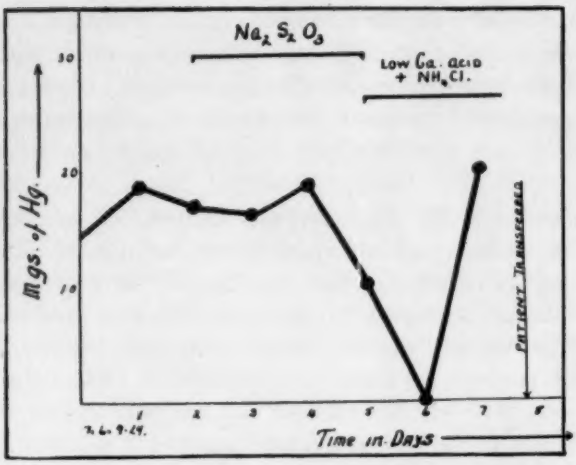

Chart 8.—Effect of sodium thiosulphate on the urinary elimination of mercury (mercury poisoning case).

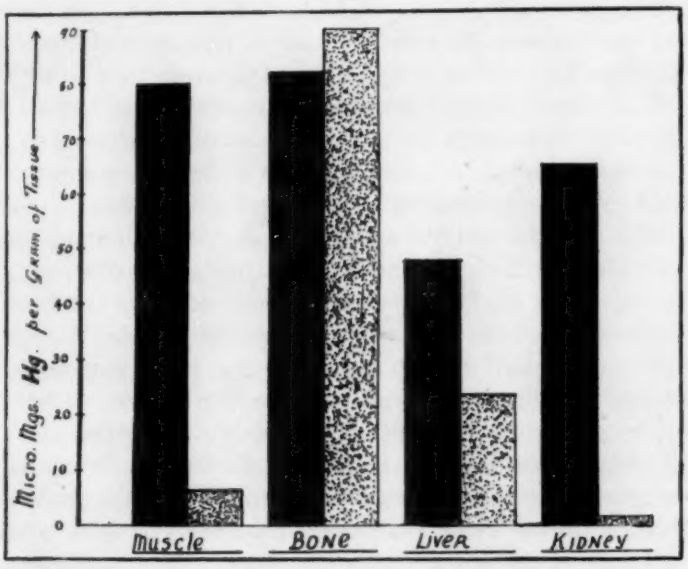

Chart 9.—Distribution of mercuric salicylate in the tissues. The solid columns represent the mercury during the period of active urinary excretion; the shaded columns, that during the period after the excretion of mercury in the urine had stopped.

muscle and kidney show only a trace of mercury. The concentration in the liver decreases about one-half, while the concentration in the bone apparently remains unchanged.

We were unable to demonstrate mercury in the brains of rabbits; but since it has been demonstrated in the cerebrospinal fluid of patients, this negative observation should not be given a final interpretation.

COMMENT

A comparison of the chemical properties of lead and mercury shows that these two metals have many reactions in common. This similarity is so striking as to suggest that they might react in much the same way in the animal organism. It was this idea that prompted the study of the effect of the ingestion of calcium (alkali) and of acid (ammonium chloride) on the rate of mercury elimination. Obviously, much work remains to be done on this subject, but we believe that the data presented here justify the conclusion that a diet rich in calcium (or alkali) diminishes, while one containing much acid (ammonium chloride) increases, the rate of elimination of mercury, the response being much more pronounced to acid than to alkali. These experiments were conducted after the method of Aub, Fairhall, Minot and Reznikoff [8] in their studies on lead poisoning and are comparable with their observations concerning the excretion of lead. It would appear at present, however, that mercury does not respond as rapidly to the ingestion of alkali as does lead. This might be predicted from a study of the difference in the amphoteric properties of the two compounds. Chart 5 gives data which show that the administration of large doses of calcium lactate are not sufficient to inhibit completely the excretion of mercury, in contrast to the complete inhibitory effect of similar doses on the excretion of lead. Further studies will be necessary to determine how completely the excretion can be inhibited by the administration of alkali and how completely the mercury can be removed from the body by the administration of acid. However, it would appear that in acute mercurial intoxication the kidney, liver and other organs might be spared if the patient were given large amounts of calcium and thereby allowed to excrete the mercury more slowly. Experimental work to verify this inference is being conducted. Conversely, it would appear that during active medication with mercury its storage might be retarded by prohibition of the use of foods rich in calcium or other alkalis.

In contrasting the rate of excretion of the water-soluble and water-insoluble compounds of mercury, it would appear that the water-soluble ones should be given therapeutically in repeated small doses,

8. Aub, J. C.; Fairhall, L. T.; Minot, A. S., and Reznikoff, P.: Lead Poisoning, Medicine **4**:17, 1925.

and that the total dose should be smaller than for the insoluble compounds. Thus, in a comparison of the excretion of mercuric salicylate and potassium mercuric tetraiodide, one notices that the tetraiodide reaches its highest rate of excretion on the fourth day, while the excretion of the salicylate gradually increases up to the ninth day. Since the mercury is brought into contact with the tissues during the period of active excretion (chart 8), one may conclude that a dose of the salicylate each week would be just as effective as daily doses of a soluble compound. It was found that the excretion of yellow mercurous iodide given by mouth varied greatly with the individual patient, some apparently absorbing very small amounts. The patients who did absorb it, excreted it in a manner comparable to that excreted after injection of potassium mercuric tetraiodide. This may be explained by the fact that yellow mercurous iodide probably becomes a water-soluble compound before it is absorbed. It is possible that the diet may be a factor in determining the amount of this iodide which is absorbed.

When the subject was placed on an ordinary well balanced diet, it was noticed that the daily excretion of mercury in the stools varied greatly, but was much lower than the urinary excretion (chart 2). This was pointed out formerly by Cole, Gammel, Rauschkolb, Schreiber and Sollmann [9] in their study of mercuric sodium bromide. When acid was administered, however, the fecal excretion increased tenfold while the urinary excretion was increased only three and one-half times. This observation is important, since it should be possible to prevent storage of mercury and obtain the same therapeutic effect by giving the patient an acid diet, fewer injections and a smaller amount of mercury.

Mercury was demonstrated quantitatively in the cerebrospinal fluid following the administration of all four of the compounds studied. Presumably, in this fluid the mercury exists as a freely soluble compound, since it is probably present there as a diffusate from the blood. This is indicated by the fact that it is possible to deposit the mercury of the spinal fluid on the electrode without previous digestion. This suggests that it was not in an organic form, or if so that it was loosely bound. In contrast, we have found it necessary to digest the urine to obtain complete yields of mercury; and, since it is difficult to digest at low temperatures and the mercury is volatilized at higher temperatures, we have found it difficult to demonstrate the mercury in the blood. The serum shows only a trace of mercury when the urine shows relatively large quantities. The concentration of mercury in the spinal fluid increases in direct proportion to the number of doses and

9. Cole, H. N.; Gammel, J. A.; Rauschkolb, J. E.; Schreiber, N., and Sollmann, T.: Excretion of Mercury After Intramuscular Injection of Mercuric Bromide, Inunction and Rectal Suppositories, Arch. Dermat. & Syph. **14**:683 (Dec.) 1926.

the amount of mercury given when soluble compounds are used. Apparently the same concentration can be obtained by single weekly doses of mercuric salicylate, but further work is necessary to confirm this tentative observation.

The studies presented here show that during the period of active excretion the mercury content of the tissues is relatively high, but that following this period the bone and, to a less extent, the liver act as a reservoir for the unexcreted mercury.

Obviously this phenomenon is affected by the p_H of the blood and tissues. Changes in diet, the administration of alkalis such as sodium thiosulphate, fever or strenuous muscular exercise undoubtedly exert an influence on the rate of elimination. One patient who had been taking a diet high in calcium and whose urinary excretion was very low showed a marked rise in urinary mercury during a reaction to arsphenamine marked by anorexia and fever. It has been impossible, even during the administration of acids, to make the patient excrete within from seven to ten days all of the mercury obtained from a single injection. During the administration of alkalis such as calcium or sodium thiosulphate, the period of excretion is even more prolonged. The bone and liver serve as a reservoir for the unexcreted mercury. Obviously, prolonged administration of mercury, especially when the subject is on an alkaline diet, results in the deposit in the body of a large amount of mercury, which may be released suddenly by any reaction which lowers the p_H of the blood or tissues. This is a potential source of mercurial intoxication. It is desirable, therefore, to control the diet of the patient during the administration of therapeutic doses of mercury, and in mercury intoxication to force alkalis and fluids.

CONCLUSIONS

1. The ingestion of acids increases the rate of excretion of mercury, while the opposite effect is obtained by the ingestion of calcium (alkali).

2. Insoluble mercury compounds injected intramuscularly are excreted over a more prolonged period than are the soluble compounds.

3. Soluble and insoluble mercury compounds penetrate into the cerebrospinal fluid in demonstrable amounts.

4. Mercury is stored in the bones and to a lesser extent in the liver. This is influenced by the p_H of the diet and the administration of acids or alkalis.

ABSTRACT OF DISCUSSION

DR. MYERS, Portland, Ore.: The mercurial compounds have been classified pharmacologically according to their clinical usage as antisyphilitics, antiseptics and cathartics. This classification has been an acknowledgment of our lack of understanding of the distribution and fate of these drugs after absorption. We have been in need of an analytic method to show what has happened to the

mercury in the body, such as Dr. Young and his collaborators have given. The excellent method of Booth, Schreiber and Zwick has been rather complicated for common use. It is particularly interesting to note that the results which Dr. Young has obtained with mercury closely coincide with those that have been obtained by Aub and his collaborators with lead. This lends strength to the observations in each instance. The results of giving an alkali or an acid are of considerable importance in therapeutic application: in aiding the distribution and holding within the body tissue, or in increasing the excretion of, mercury. This will be important not only in the therapy for disease but also in the treatment of persons with mercurial poisoning. The results that Dr. Young has obtained with sodium thiosulphate are decidedly interesting and agree with the results of others in the increased excretion of drugs in which thiosulphate has been used.

We are all greatly indebted to Dr. Young for this distinct addition to our understanding of the fate and distribution of the mercurials.

DR. HANZLIK, San Francisco: I was much interested in this paper, because of the interesting effects of salts, the apparent differences in salt effects on mercury and bismuth and the high permeability of the central nervous system to mercury.

Dr. Young finds that the chlorides of calcium and ammonium increase the urinary output of mercury, but thiosulphate does not. The recent work of Garcia in Munich somewhat fits in here, although the salts and mercury compounds employed were different. Garcia found that such salts as the chloride, bromide and iodide of sodium increased the mobilization of insoluble depots and the toxicity of mercury in rats. Garcia attributes these effects to the solubility actions of the haloids. Consequently, it would appear that caution should be exercised in the use of salts in treating patients with poisoning from mercury, because the symptoms of poisoning might be aggravated owing to increased solubility and increased concentration of mercury in circulation.

In our studies of bismuth, we have found that a number of salts, thiosulphate included, whether they liberate acid or not, increase its excretion. Production of a high temperature by a bath, malarial fever and vaccines also increase the excretion of bismuth. We know that bismuth is distributed differently than mercury; it is selectively deposited in the kidneys and not in the bones, as is mercury. This difference may account for the differences in the salt actions on these metals.

Another factor is the apparently high permeability of the central nervous system to mercury. Dr. Young tells me that he finds as much as 0.5 mg. of mercury in from 25 to 50 cc. of spinal fluid after intensive medication. On the other hand, all reports point to the absence or mere traces, of bismuth, in the cerebrospinal fluid, except in animals with meningitis. Here again there would seem to be a difference between mercury and bismuth.

DR. YOUNG, Cambridge, Mass.: I wish to say only that Dr. Hanzlik is correct in saying that I have found 0.5 mg. of metallic mercury in the cerebrospinal fluid after the usual clinical dosage. This occurred regardless of what substance we gave. Some of the patients were not syphilitic but were being treated for some other condition and could be given mercury without injury. Therefore, the penetration could not be attributed to injury such as one finds in meningitis.

The penetration of the mercury, I believe, is influenced by various salts. Potassium iodide and ammonium salts greatly increase the rate of diffusion of the mercury.

THE LIVER IN ACTIVE SYPHILIS

A STUDY OF ONE HUNDRED AND SEVENTY-NINE CASES OF CUTANEOUS SYPHILIS *

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AND
A. M. SALA, M.D.
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That the liver, a most highly vascular organ, is readily open to invasion by *Spirochaeta pallida* as it enters the blood stream at the time of its dissemination through the body, is well known.

In the early stages of the disease, the cells that are susceptible to the specific toxin undergo variable degrees of degeneration. Besides the usual pathologic picture of syphilis, there is an acute vascular reaction with an associated swelling of the fine biliary ducts. The body, in an effort to destroy the spirochetes that continue to survive in spite of the high degree of resistance encountered at the end of the secondary stage, causes the production of a fibrosis. When the tissues have failed at this process, necrosis ensues, with the formation of gummas. Irrespective of the treatment instituted, these necrotic lesions tend to heal by a secondary fibrosis. According to Symmers,[1] the tissues have a tendency to an overproduction of fibrous tissue, this process being most marked in the liver.

The excretion of bilirubin is one of the functions of the liver. If the liver is unable to do this properly, the pigment is retained, and a hyperbilirubinemia results. In the absence of extraneous factors producing excessive bilirubin in the blood stream, this hyperbilirubinemia is in direct proportion to the extent of dysfunction of the liver. It was our endeavor for the purpose of our study to detect this increase of circulating bilirubin with tests that could be simply and rapidly performed. We selected the qualitative van den Bergh and icterus index tests. In the presence of degeneration of the liver of sufficient proportions, the van den Bergh test will give a positive direct delayed reaction. In other words, on the addition of the diazo reagent to the blood serum, the typical change in color will be seen after one or more minutes.

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* Submitted for publication, Sept. 18, 1929.

* From the Department of Dermatology and Syphilology and the Pathological Laboratory of Harlem Hospital.

1. Symmers, D.: Anatomical Lesions in Late Syphilis, J. A. M. A. **66**:1457 (May 6) 1916.

The icterus index does not actually determine the amount of bilirubin present, but by comparing the color of the blood serum with a standard, an increase or decrease can be readily detected; the result is supposed to be reliable for clinical purposes.

What is the effect of the spirochetal toxin on the hepatic cells? This must be considered, first, from the standpoint of the patient and second, from that of the clinician. Does it present a more complex and varied problem as regards the treatment of the syphilitic patient? The invasion of tissues by an organism does not necessarily mean the production of a pathologic process; that, of course, depends on the degree of local resistance and the virulence of the offending organism.

The purpose of this investigation was to acquire information concerning the following points: (1) the percentage of cases in the various stages of syphilis in which a hepatitis develops; (2) the influence of arsenic, in therapeutic dosage, in the presence of hepatic injury; (3) the percentage of cases with liver damage in which clinical jaundice develops and (4) whether it is clinically possible to predicate hepatic injury before the onset of jaundice.

There were 179 cases of cutaneous syphilis under observation. In no instance was jaundice detected on admission; the patients sought relief solely for the cutaneous eruption. A positive direct delayed van den Bergh reaction was observed in forty-five, or 25 per cent, of the total number of cases. A reaction of maximum intensity was seen in 50 per cent of the positive cases after from ten to thirty minutes and in 50 per cent at the end of the hour. Of a total of 118 cases of secondary syphilis, there were twenty-one positive reactions, or 17 per cent. In fifty cases of tertiary syphilis, there were twelve positive reactions, or 24 per cent. Of the eleven cases of primary syphilis, there were four positive reactions; the total number of these cases is too small for detailed consideration.

This seems to show that the liver is involved in all stages. Stokes [2] said that syphilis of the liver should be common and that the incidence of early reaction is probably high. Symmers,[1] in a series of autopsies on patients with proved cases of syphilis, found the liver involved in 33.4 per cent of his cases. We feel that many more cases of hepatitis were present in our series, but the dysfunction was so slight as to prevent detection. Wile [3] expressed the opinion that syphilis of the liver is undoubtedly far more frequent than is generally supposed, especially when one considers that many cases do not give rise to clinical

2. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1926, p. 768.

3. Wile, U. J.: Syphilis of the Liver, Arch. Dermat. & Syph. **1**:139 (Feb.) 1920.

symptoms. The great majority of our patients had no complaints referable to the liver. Of a total of forty-five patients, only two complained of a weak feeling in the epigastrium, slight nausea and eructations of gas; these symptoms were elicited only after close questioning. Under no condition could a clinical diagnosis of hepatitis be made in any of our cases. The incidence of syphilitic hepatitis was greater in the tertiary than in the secondary cases. This result is to be expected, since the fibrosis and the more widespread degeneration of the liver cells of the late stage could readily account for it.

The incidence of positive reactions in primary syphilis is surprisingly large, showing that at least a hepatitis of a mild degree can be seen in the initial stage. In one of our cases, a positive reaction of maximum intensity was observed in fifteen minutes. According to the patient's history, which seemed reliable, the chancre was present only one week. That syphilis becomes a generalized infection early there is no doubt, but the probability of a complicating hepatitis in the primary stage was entirely unexpected.

The results of the icteric index tests must be considered in the light of technical difficulties. An effort was made to perform the tests under ideal conditions, but this was impossible in many instances. The following sources of error will interfere with the accuracy of the results: (1) hemolysis, even of a slight degree; (2) withdrawal of blood soon after a meal and, (3) allowing the blood to stand more than twelve hours before testing. According to the observations of the various investigators, normal results range between 4 and 6. An index above 6 and below 15 is supposed to indicate latent icterus. In forty-five cases with positive van den Bergh reactions, the icterus index was above 6 in all but four instances, and these ranged between 4 and 6. We did not consider significant an icteric index above 6 when the van den Bergh test was negative. It is our opinion that the determination of the icterus index alone for the detection of mild dysfunction of the liver is not entirely reliable, and other tests, such as the van den Bergh, should be employed in addition.

It is interesting to note that of 134 patients with negative functional tests, sixteen or 12 per cent gave positive reactions following treatment. As far as we could determine, none of these developed jaundice.

Granted that mild degrees of hepatitis are fairly prevalent, at least in active syphilis, we were anxious to learn in how great a percentage of cases in our series the condition was merely intensified under treatment and in what percentage clinical jaundice ensued. The arsphenamine compounds, after leaving the circulation, are stored chiefly in the liver. It is natural to assume that a pathologic process in the presence of an irritant such as arsenic will become aggravated.

Our routine procedure was to administer neoarsphenamine intravenously in doses of 0.45 Gm. at weekly intervals. One week after the fourth and eighth treatments examinations of the blood were made for detection of liver damage. Whenever a positive van den Bergh reaction was obtained, the patient received the maximum therapeutic dose of 0.9 Gm. of neoarsphenamine. The purpose of giving maximum dosage was to determine whether it was possible to activate the pathologic process to such an extent that it might be recognized clinically.

Since it is difficult in clinic practice to have patients return at regular intervals for treatment, only twenty of the forty-five patients with positive reactions received four or more treatments. Twelve patients received a full course of eight injections of neoarsphenamine of 0.9 Gm. each. Of the twelve receiving the full course of injections, the van den Bergh reaction became more intense in six instances; in other words in 50 per cent of the number, the reaction appeared sooner and became more marked. Of the eight patients receiving from four to seven treatments the reactions remained positive in three but were not intensified. In 35 per cent of the original positive cases the reaction became negative when the patient was under treatment with maximum doses of neoarsphenamine.

Two patients developed clinical jaundice, one during treatment and the other five months after the last injection. The first was that of a patient with an initial lesion; a Wassermann reaction of the blood of 4 plus; a direct delayed van den Bergh reaction in fifteen minutes; and an icteric index of 13.6. A few days after the third injection of neoarsphenamine, the patient appeared with a faint erythematous dermatitis of the legs and face and complained of an intense generalized pruritus. On close observation a faint yellow discoloration of the sclerae was observed. The van den Bergh was strongly positive at two minutes and the icterus index was 16. The itching became more intense the following two days in spite of treatment with sodium thiosulphate; all symptoms, however, soon abated, and within ten days the patient was free from all complaints, the jaundice having also disappeared. Two months later, the van den Bergh reaction was faintly positive at ten minutes, and the icterus index was 7.5

The other case was of particular interest because the hepatitis became clinically evident five months after the last arsenical injection. On admission the patient had a tertiary nodular syphilid of both legs, of one month's duration. The van den Bergh test was faintly positive after fifteen minutes, and the icteric index was 9. The eruption improved soon after the first injection, and disappeared after the third. After the fourth treatment the icterus index was 5, and the van den Bergh reaction was faintly positive at the end of the hour. After the eighth injection the van den Bergh test was reported negative. About five months later,

the patient applied at the medical clinic for relief from epigastric distress, headache, dizzy spells and yellow discoloration of the eyeballs. The patient was referred to us for an opinion. On examination, the conjunctiva and buccal mucous membranes were slightly yellow; the liver was not enlarged. The icterus index was 18, and the van den Bergh test was strongly positive in two minutes. With the patient under treatment with sodium thiosulphate, the symptoms abated immediately and the jaundice disappeared in twelve days. Within three weeks the icterus index was 8.2, and the van den Bergh reaction was faintly positive in two minutes. Four months later the van den Bergh test was faintly positive at thirty minutes, and the icterus index was 6.75. A mild degree of hepatitis still existed, although the patient was unaware of its presence.

In only two, or 10 per cent, of 20 patients who were treated and who showed some form of dysfunction of the liver, did the hepatitis advance to such an extent as to be recognized clinically. As a result of this experience we must conclude that in the presence of a mild syphilitic hepatitis, arsenical compounds are not absolutely contraindicated but should be given with caution. Even if the van den Bergh reaction is reversed to negative, dysfunction of the liver may still be present, though slight, and at any moment it may become aggravated by some unforeseen condition.

Why is it that a syphilitic hepatitis with added insults from arsenical medication will not become more extensive in a greater percentage of cases? As far as we were able to determine, the condition in 35 per cent of the cases cleared after treatment was instituted. We are of the opinion that the patient must be hypersensitive to arsenic in order to develop an advanced degeneration of the liver under therapeutic dosage. Which patients are hypersensitive to the drug no one can say, but it is obviously essential that if hepatic dysfunction is once detected, that patient must be kept under observation not only during treatment but also months after, even if the functional tests have become normal. A hepatitis of a mild degree may exist in spite of negative tests. If a patient complains of epigastric distress before or during the course of treatment, tests to determine the function of the liver should be performed to rule out the possibility of an existing hepatitis.

We do not contend that the patients in 10 per cent of the cases showing some form of hepatitis will eventually develop jaundice, but we do assert that if the patient cannot be kept under close clinical observation, an antispecific such as bismuth, which is less toxic to the liver, should be employed instead of arsenic. Particular attention should be given cases of late syphilis, for these have a greater tendency toward advanced hepatitis.

SUMMARY

1. In a series of 179 cases of cutaneous syphilis, 25 per cent had a positive direct delayed van den Bergh reaction. It occurred in 17 per cent of cases with secondary syphilids; 24 per cent of cases with tertiary syphilids and in four cases with initial lesions.

2. In all but four instances, of forty-five cases with positive van den Bergh reactions, the icterus index was above 6, and in these the results ranged between 4 and 6. In many of our apparently normal cases, the icterus index was above 6.

3. In 12 per cent of 134 cases with negative reactions, the van den Bergh reaction became positive while the patients were under treatment; clinical jaundice, however, did not develop in any of these.

4. Only 10 per cent of the twenty patients with positive reactions who were receiving from four to eight treatments developed clinical jaundice, in spite of a maximum therapeutic dosage.

5. In 35 per cent of the positive cases, the reaction became vegetative during treatment.

CONCLUSIONS

1. The van den Bergh test is a rapid and accurate method for the detection of hepatitis.

2. An icterus index above normal is not an indication of an existing hepatitis, unless it is confirmed by a positive van den Bergh reaction.

3. A syphilitic hepatitis may be present in all stages of the disease. The incidence is greatest in the tertiary stage.

4. Mild cases of hepatitis do not present symptoms. In all cases presenting gastric disturbances during arsenical medication, tests should be performed to determine the function of the liver and to detect the possibility of an early hepatitis.

5. The presence of a mild syphilitic hepatitis is not a contraindication to arsphenamine therapy, although all patients must be kept under strict observation. Ten per cent of the patients in our series developed jaundice.

FACTORIAL CONCEPT OF HEREDITY IN RELATION TO DISEASE, ESPECIALLY SKIN DISEASE*

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The science of genetics has been revolutionized within little more than a quarter of a century. It is no exaggeration to say that more real insight into the mechanism of heredity has been obtained since the rediscovery of Mendel's Law in 1900 than had been acquired in all preceding time. As a result of this rapid advance, few except specialists in genetics have an adequate realization of the changes that have been made in this field. Many concepts have been abandoned and new points of view have been introduced, so it is not surprising that many who write on heredity should still continue to interpret their facts in terms of the outgrown categories of a previous generation.

Following Mendel, geneticists have focused their attention on the transmissions of particular characteristics appearing to behave as units, which can be combined and separated in almost any possible relation. Hence, the expression, "unit characters," which was in vogue in the early years of mendelism. At that time, an individual was looked on as a collection of unit characters, each of which might be replaced by another unit character without altering very much the rest of the organism. But fuller experience with mendelian phenomena has led geneticists to abandon the notion of unit characters. Strictly speaking, characters are not transmitted at all. What is passed on in the germ plasm is rather a set of inheritance factors, or what are now called, genes. These genes are doubtless located in the chromosomes, where, as Morgan and his pupils have shown, they probably have a definite linear arrangement.

It is wrong to assume that each gene is solely responsible for the character for which it stands. Genes are factors which in combination with multitudinous other genes, and in the presence of a suitable environment, produce specific effects on the development of the organism. Alter a gene, and the organism is changed perhaps only in a single feature of its structure. Every character is, nevertheless, the product of numerous genes, and each gene may affect to a greater or less extent a number of characters, although usually its influence is most conspicuously expressed only in one part. Genes are differential

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* Edited and read before the American Dermatological Association by C. D. Leake.

factors. A single factorial change may make the difference between a normal and an ichthyotic skin, although either condition is determined by other genes and probably by other influences (such as environment) besides.

Some people may look on a gene as standing in the same relation to a part which it influences as a seed to a plant. This view follows the traditional conception of heredity as passed down from the Greeks. But it is doubtless quite wrong. A gene is a factor that produces a given result in development through a long chain of intermediate happenings, each of which is influenced by many other genes. Genes may therefore cause their effects in a roundabout way. An excellent illustration of this has been indicated by the experiments of Bagg,[1] on the production of hereditary effects in mice by the action of roentgen rays. Among these was a condition of syndactylism resembling clubfoot, which proved to be inherited through several generations. One might conclude, according to Weismann, that leg-forming genes had somehow been affected by the treatment. If so, the defect was produced in an unusual way. The earliest alteration observed in the developing limb was the formation of a blister-like bleb which raised the epithelium of the foot. This was followed by the accumulation and frequent clotting of blood in the area. This seemed to act as a disturbing factor in the development of the limb, and sometimes prevented its formation entirely. The immediate cause of the anomaly seemed to be the extravasation of blood and lymph. If one could locate the cause of these blisters, one might find it in some quite different bodily change, say in the physical-chemical balance of the cells involved, which in turn might be the result of the influence of other altered genes.

In order to understand the manifold effects of single hereditary factors, we should study their effects during the process of embryonic development. At present there seems little correlation in these effects. In man, for instance, there is a curious association between hereditary fragility of bones and a peculiar bluish color of the sclerotic coat of the eye. Again, the factor that causes the coat color in mice to become yellow also causes the death of the animal if present in a double dose.

The fact that genes produce many different effects carries the corollary that each character is the product of many genes. Hence, variations in any part may be produced to a greater or less extent by a number of mutations in different genes. This important fact has been abundantly demonstrated in the fruit fly. A hundred or more mutations in eye color have occurred in this form, a considerable proportion of which are known to be due to gene mutations in different

1. Bagg, H. G.: Hereditary Abnormalities of Limbs: Their Origin and Transmission, Am. J. Anat. **43**:167 (March) 1929.

loci in the different chromosomes. Often variations of a similar kind are caused by changes in quite different genes. Such changes make possible the discovery of two kinds of factors of related influence, called multiple factors and modifying factors. The recognition of these classes of factors has contributed much toward elucidating many heretofore puzzling phenomena of heredity by making it possible to bring them under the general scheme of mendelian heredity. The recognition of multiple factors at once enabled geneticists to give a plausible explanation of blending heredity, as illustrated by the color of the skin of mulattoes, in terms of Mendel's Law. The multiple factor hypothesis has recently been employed by Macklin to give a plausible interpretation of the puzzling phenomenon of mongolian idiocy.

The circumstance that similar effects are sometimes produced by different factor mutations enables us to interpret the fact that in human beings that which appears to be the same trait is sometimes inherited in different ways. A survey of numerous pedigree charts of the transmission of human traits affords many instances of this varied method of hereditary transmission. A character is dominant, recessive or sex linked. The form of partial albinism revealed by a white patch above the forehead, is usually inherited as a simple mendelian dominant. A few years ago, Schofield and Holmes traced a pedigree through several generations in which the trait appeared only in males, although it was transmitted through females who did not exhibit it. In another family, Dr. Schofield found that the character of webbed toes was inherited as if it were carried by the Y. chromosome, although in other families a similar condition is transmitted without any relation to sex. Several conditions of the skin appear to exhibit a similar diversity in their modes of inheritance.

If one compares human heredity with that of animals whose genetics have been fully investigated, it would seem that there is considerably more diversity in the ways in which traits are carried on in man than there is in most other organisms. Human beings constitute probably the most heterozygous type of known animals. A part of the diverse modes of man's inheritance is probably due to this cause, since the same factorial change may exhibit itself quite differently, owing to its association with different factor complexes.

On account of the diverse heredity of human traits, it is hazardous to try to interpret all cases of feeblemindedness, epilepsy and insanity as due to the same factorial modification, and therefore as inherited according to a simple mendelian ratio. Incomplete and variable dominance is commonly observed, and this fact should be kept constantly in mind in interpreting the heredity of human defects and diseases. The characters studied by Mendel were sharply either dominant or recessive. As more cases of mendelian heredity were

investigated, more and more cases of incomplete and variable dominance were brought to light. Both the dominant and the recessive factors may be regarded as struggling for expression during the development of the organism. One factor may suppress the other entirely, or each may reveal its influence in producing an intermediate condition. Again, the outcome may vary, owing to the coincident influence of the environment or other associated hereditary factors, and thus results a great variability in the appearance of a given character. Polydactylism is a characteristic of this sort, whether it occurs in human beings, guinea-pigs or domestic poultry. The trait is sometimes expressed in one or both hands or in the feet, and in various degrees. Persons with polydactylous parents may not show the characteristic at all, although they can transmit it to their offspring. It is uncertain whether such persons are normal because of favorable environmental conditions in early development or because of the influence of other hereditary factors.

Cases in which dominance is modified by the environment are more common. The character of abnormal abdomen in the fruit fly is a definite mendelian trait, and it regularly appears generation after generation, but only under the proper conditions. Bred in a dry environment, the flies exhibit a normal appearane, but these apparently normal flies are capable of giving rise to abnormal progeny under unusual conditions. In a truly normal stock of flies, no environmental condition can produce the abdominal abnormality. This strain of fly is differentiated from the rest of the species by the possession of a gene which may or may not produce an abnormal abdomen, dependent on environmental factors. A somewhat similar situation may exist in certain skin conditions, such as epidermolysis bullosa, or in some cutaneous allergic phenomena which seem to have a hereditary factor.

When we find hereditary traits skipping a generation now and then, as they often do, and manifesting themselves in varying degrees, they are not unlikely to prove to be imperfect dominants whose expression requires some other influence. A striking instance of fluctuating dominance is furnished by club wings in *Drosophila*. This characteristic appears in about 20 per cent of the fruit flies in which the gene is present. Since it is associated with another manifestation of the same gene, namely, the absence of bristles on the side of the thorax, it is possible to trace its heredity by observing the conditions of the bristles, since the latter character always appears when the gene is present. The fluctuation of dominance thus affects only one part of the expression of the gene. Were it not for the association of clubwing with the absence of thoracic bristles, it would be difficult to understand the heredity of this wing anomaly. If such a variable trait occurred in

man, it would be almost impossible to trace its mode of inheritance or even to prove that it was inherited.

These genes vary greatly in what we may call their self-assertiveness. Some are modest and retiring, giving rise to typical recessive traits. Others, such as the so-called intensifying and diluting factors, exercise a mild influence on the expression of other genes. Some are obstructionists, like the dominant gene which prevents the development of horns in cattle. Others, the lethals, interfere with the developing embryo and cause death at various stages from the germ cell to the adult. These genes are self-propagating little entities which for the most part work together in harmony, but their disagreements sometimes transgress the bounds indicated by the conflict of dominant and recessive factors and cause all sorts of hereditary anomalies. If a gene causes development to go too far away, it thereby becomes a lethal factor. It is a noteworthy fact that the great majority of gene mutations caused in the fruit fly by the application of roentgen rays produce lethal factors. A considerable number of these are known and properly located in the chromosomes. It is also noteworthy that the majority of the several hundred mutations that have appeared in the fruit fly during the past twenty-five years are relatively unfavorable from the standpoint of survival. In other words, most variation is bad, from the standpoint of organic welfare. Most variations are also recessive, thus indicating that their factors have a reduced power of what we have called their self-assertiveness. To the extent, therefore, that a species is shielded from the action of natural selection, it tends to carry along a number of defective modifications. Our own species appears to be particularly burdened with defective modifications. The failure to eliminate such variations probably constitutes one of the reasons for the great diversity of hereditary traits which our species exhibits.

Since the expression of genes is so frequently conditioned by other hereditary factors as well as the environment, organisms often fail to manifest the traits for which they have the hereditary basis. It is often said that one cannot escape heredity. At the time of fertilization heredity is fixed and unchangeable, but nevertheless one can often escape falling a victim to it. Speaking broadly, one does not necessarily have to have traits because one inherits them. People commonly look on heredity as something fatalistic. Correlated with this common notion is the conclusion that if a malady can be prevented or cured by any sort of treatment, heredity cannot have been in any way responsible for its occurrence. In treatises on medicine, one often finds statements as to the percentage of cases of certain disorders caused, it is said, by heredity. The common assumption is that the malady is caused either by heredity or by some other factor. As a matter of fact, in a large

proportion of cases, the trouble is due to both. When an environmental factor is shown to be indispensable for the production of a given malady, it is quite unjustifiable to deny that heredity may be an essential factor at the same time. There has been no end of confusion over this relatively simple matter. Nowadays, most intelligent physicians would not deny the possible importance of heredity in the development of tuberculosis simply because this disease cannot develop in the absence of the tubercle bacillus. Different strains of guinea-pigs, as Wright has shown, differ considerably in their proneness to contract tuberculosis, and different strains of mice differ even more sharply in their susceptibility to pneumonia. The tendency to divide maladies categorically into hereditary and nonhereditary groups has resulted in much confusion and misunderstanding.

It is probable that racial heredity predisposes different races to certain diseases. White persons are more liable to contract scarlet fever, diphtheria, measles and erysipelas than the negroes. The negro, in fact, has a peculiarly resistant ectoderm. Cancer of the skin, buccal cavity and mammary gland is relatively rarer among negroes than among white persons, but in cancer of the uterus, the relations are reversed. The negro also enjoys marked immunity to psoriasis.

The importance of hereditary predisposition to infections as well as other types of disease is coming to be more clearly recognized than it was some years ago. It has been definitely demonstrated in numerous instances in plants and animals, and everything one knows about human heredity indicates that it follows precisely the same laws that obtain among other species than our own. From the nature of the case, the investigation of modes of inheritance in human traits presents many difficulties. But animal experimentation may show us what to expect in man. If, for instance, controlled experimentation reveals the mode of transmission of the diathesis to tuberculosis, pneumonia, cancer and other maladies in guinea-pigs and mice, one may not be entirely justified in assuming that these traits will follow the same rules in man. We can at least ascertain whether the data on human heredity fit into the same scheme. To obtain real insight into the relation of diathesis to disease, one must employ controlled animal experimentation and correlate it with reliable human records.

This may be a very fruitful study in connection with certain skin conditions. Maud Slye's remarkable experiments appear to prove that cancer, at least in her mice colonies, is determined by hereditary factors. The attempt to obtain reliable human data for correlation with her results deserves the most careful attention.

Many disturbances of the skin, such as albinism, allergic manifestations, angioneurotic edema, epidermolysis bullosa, hypotrichosis,

ichthyosis, monilethrix, and tylosis seem to be conditioned by hereditary factors. There are not reliable enough histories of afflicted families to enable one to estimate the significance of these factors. The difficulty of determining their dominant, recessive, or sex-linked qualities may be a reflection of the propositions discussed previously. At any rate, the matter deserves systematic and controlled study, especially if there is to be any rational background for sound eugenistic advice in the efforts to control the future incidence of these conditions.

For this reason there should be a central repository for the collection and study of such records as may be obtained. The Cold Springs Harbor Laboratory is such a place, but it is not especially interested in the hereditary factors in skin disease in man. If you are really interested in this problem, perhaps a committee of your own, in cooperation with some competent geneticist, may satisfactorily evaluate such data as you secure.

SUMMARY

A brief survey has been made of the factorial concept of heredity. The manifestations of mendelian phenomena occur through inheritance factors (genes), which in combination with many other factors, including environment, may produce specific effects on the development of the organism. The relation of this concept to disease, especially skin disease, is discussed.

Evidence exists indicating a hereditary factor in such skin conditions as albinism, allergic disturbances, angioneurotic edema, cretinism, eczema, epidermolysis bullosa, hypotrichosis, ichthyosis, monilethrix, pemphigus connatus and tylosis. Cancer seems also to be determined by hereditary factors.

Satisfactory histories of afflicted families are not yet numerous enough to estimate the dominant or recessive qualities of these conditions, or the influence of sex linkage. It is important to study this problem intensively in order to be able to control the future incidence of these conditions by eugenistic advice. It is suggested that the American Dermatological Association establish a committee for the collection and evaluation of information dealing with the hereditary aspects of skin disease.

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GRANULOMA SENILIS *

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In 1927, Kreibich reported a case of what he called granuloma senilis, in which the following history was given.

A woman, aged 55, had had about fifty typical warts on her back for many years. During the last three months, two of them had ulcerated and appeared as red nodular elevations, one as large as a hazelnut, the other the size of a pigeon's egg. After removal of a brown crust, an irregular papillomatous surface was seen which on one edge was continuous with a senile wart. It was diagnosed as carcinoma of a senile wart and was excised. Histologically, there was a definite epithelial margin of basal cells. With the exception of the superficial ulceration and edema of the rete pegs, the section was similar to that of the adjacent senile warts. In calling this lesion a granuloma senilis, Kreibich pointed out that the name indicates a granuloma of a senile wart and not a granuloma of the senile skin.

The following case is reported as being similar, and as far as can be determined, it is the second one to be described.

REPORT OF CASE

History.—A man, aged 77, came to the surgical clinic of the New Haven Hospital with a small lobulated and partially encrusted tumor just posterior to the lobule of the left ear. In childhood he had had large numbers of warts (verruca vulgaris) on different parts of his body, but most numerously on his hands. Following adolescence, these all disappeared until several years before examination, when he noticed a group of several small warts behind the lobule of his left ear. The patient admitted having scratched them, and during the last two months this area had been partially covered with a crust, which he had often removed.

There was present behind the left ear a tumor which had a dusky red, smooth surface, the whole resembling a lobulated epulis. It was attached by a short, thick pedicle. About one fourth of it was covered by a serosanguineous crust, which on removal left a red, minutely papillary surface.

A diagnosis of infected epithelioma was made, and the lesion was completely excised. The wound healed per primam and when seen two months later showed no recurrence.

Pathologic Examination.—Gross examination showed an elliptic piece of skin 2.5 cm. long and 1.5 cm. wide containing a tumor about 9 mm. in diameter and about 4 mm. in height. It was dark red and lobulated and was set on a broad, short pedicle.

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* From the Department of Surgery, Yale University.

On microscopic examination, the epidermal layer was found to be missing over most of its external surface, but it was distinctly seen at the margin of the tumor extending part way up its pedicle. The epithelial margin was sharply defined by basal cells. These epithelial cells were uniform in regard to size, nuclei and nucleoli wherever they were found and were similar to cells in the same relative position seen in any senile wart. The rete pegs were enlarged and elongated and contained the usual amount of cellular infiltration found in any wart. Many small groups of rete cells had become swollen and vacuolated, as can be seen in the accompanying figures. Near the margin the rete pegs became shorter and less penetrating with a gradual transition to the usual size of a rete peg. Just beneath this the papillae were edematous and appeared as a delicate reticulum which was infiltrated with polymorphonuclear leukocytes, plasma cells and a few lymphocytes. The spherical or elevated portion of the tumor consisted of connective tissue cells which lay close together without any definite arrangement. Capillaries and small blood vessels were almost entirely absent. The external surface of this portion of the tumor was, in some places, covered by a thin, serosanguineous crust. Immediately beneath the main body of the tumor the subcutaneous tissue contained groups of plasma cells together with a few lymphocytes and polymorphonuclear leukocytes.

According to Kreibich, the lesion has the following sequence: Scratching by the patient causes traumatic inflammation and loss of the normal horny layer; further trauma increases the inflammation which due to lack of counter pressure of a normal horny layer produces edematous loosening, stretching and upheaval of the papillae, whereupon the epithelium responds with stretching and extension. This process, in which the extension downward of the epithelium is only apparent, corresponds to that which we find in granulomas and occasionally in acuminate condylomas. While in the granulation or granuloma of Kuttner this process takes its course without epithelium, or only on the edge under the epithelium, in this instance it develops under the epithelium of the senile wart and produces a swelling clinically and above all histologically resembling a carcinoma. This is then substantially different from the change of the senile wart to epithelioma, rodent ulcer or carcinoma.

(Der Process hat offenbar folgenden Ablauf: Kratzen von der Patientin zugegeben, führt zur traumatischen Entzündung und zum Verlust der normalen Hornschicht; weitere Traumen vermehren die Entzündung, die wegen fehlendem Gegendruck seitens einer normalen Hornschicht zur ödematösen Auflockerung, Streckung und Emporwucherung der Papille führt, worauf das Epithel mit Streckung und Dehnung antwortet. Dieser Vorgang, bei welchem die Tiefenwucherung des Epithels nur eine scheinbare ist, entspricht dem was wir beim Granulom und zum Teil auch beim spitzen Kondylom antreffen. Während er bei der Granulation oder beim Granuloma Küttner ohne Epithel oder nur am Rande unter Epithel verläuft, vollzieht er sich hier unter dem Epithel der senilen Warze und bedingt eine Geschwulst, die klinisch und zunächst auch histologisch ein Carcinom vortäuscht. Es liegt hier im Wesen etwas ganz anderes vor als bei der Unwandlung der senilen Warze zum Cancroid, zum Ulcus rodens oder zum Carcinom überhaupt.)

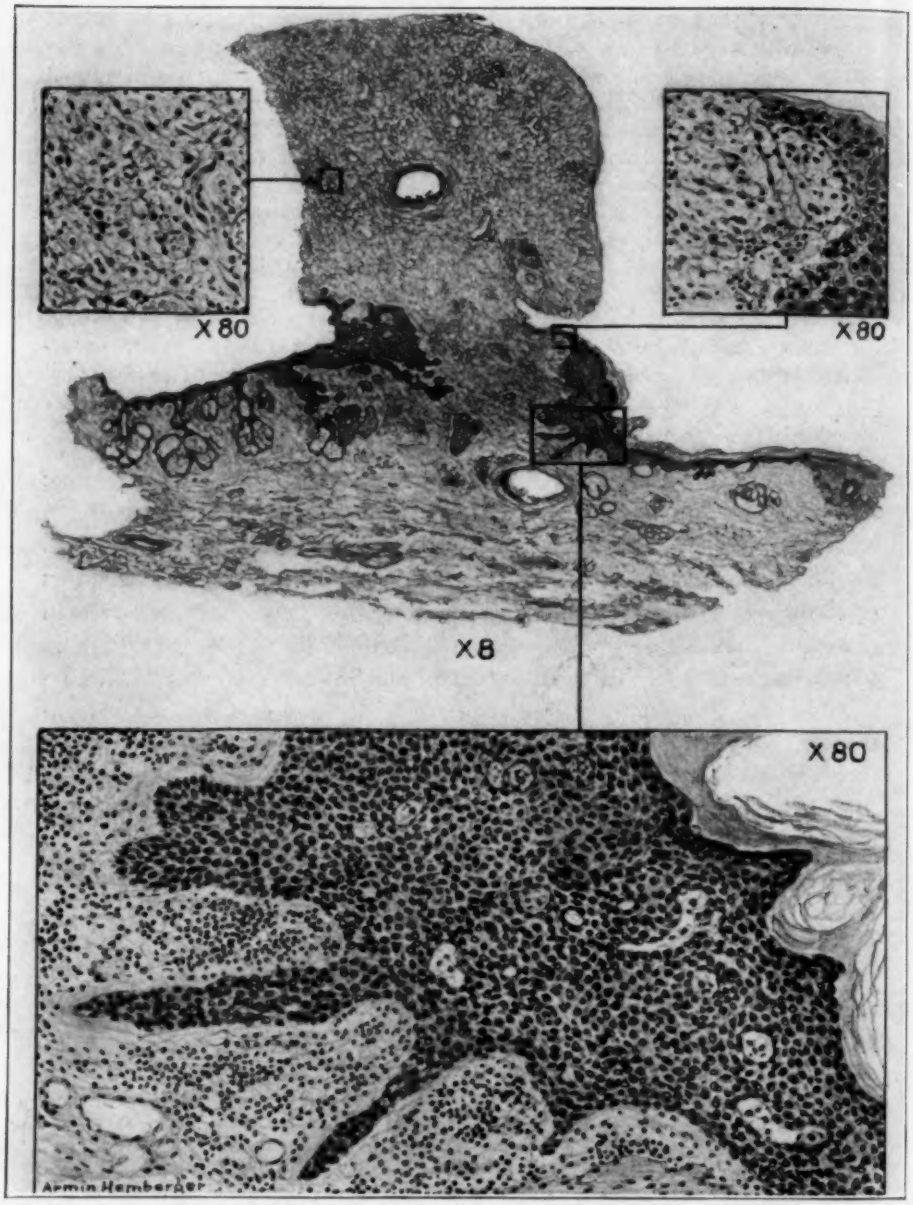

Fig. 1.—Microscopic appearance of granuloma with high power views of various portions as indicated.

Fig. 2.—Gross appearance and section of granuloma, actual size.

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The resemblance of this lesion to carcinoma has been stressed by Kreibich, and this similarity is well illustrated in the present case, in which a clinical diagnosis of a probable malignant growth was made. This resemblance was also brought out in the microscopic sections in which the first impression was that of a malignant condition.

There are two reasons which make us feel that this is not granuloma pyogenicum (or botryomycosis as it is still called by the French school):

1. There is a history of previously existing warts, which, so far as we have been able to determine, have never been associated with granuloma pyogenicum. The latter occurs most frequently following a slight trauma on previously uninvolved skin or mucous membrane.

2. Histologically, granuloma pyogenicum is vascular. In some cases, the capillaries and blood spaces are almost as numerous as in an angioma. In this case the capillaries and other small vessels were sparse. However, Michelson has shown that a wide variation exists in the number of capillaries in individual instances of granuloma pyogenicum. A similar variation might be possible in granuloma senilis since both are granulomas, but in the two cases so far reported the tumor has been relatively avascular.

SUMMARY

An instance of granuloma senilis was described by Kreibich in 1927. A second case is reported by us.

The condition occurs following trauma and resembles a malignant change in a senile wart. It must be differentiated from epithelioma and granuloma pyogenicum.

The name granuloma senilis indicates a granuloma of a senile wart, and not a granuloma of senile skin.

MADURA FOOT

ITS HISTOLOGY AND MYCOLOGY *

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In Dutch Guiana mycetoma pedis is a rare disease. Until the present, no case has been reported.

REPORT OF A CASE

History.—A British Indian woman, a laborer, aged 41, born in Surinam, came under my care in November, 1928. She had a tumor-like, suppurating swelling of the left foot, which had been present for about two years. The process started with a painless nodule which appeared on the dorsum of the diseased foot. It showed little progress during the first year. Gradually more nodules manifested themselves, and superficial ulceration of parts of the nodular mass took place. I could not obtain a reliable history about previous trauma, or the further course of the disease. Because of pain in walking, the patient sought medical treatment and was admitted to the Military Hospital at Paramaribo. There was no history or evidence of syphilis or yaws.

Examination.—The patient appeared to be in good health; the general nutrition was good. Internal examination revealed nothing of note. The results of urinalysis were negative, as were the Kahn and Meinicke reactions. Serologic tests with *Actinomyces* or *Sporotrichum* antigen were not performed. In the groins there were slightly enlarged lymph glands; in the tropics, however, this is not unusual, as the barefooted laborers suffer from many lesions.

The dorsum pedis was deformed by a more or less uniform swelling, in which a number of nodules of different sizes could be observed. In the center of the tumor there was a round, depigmented scar, caused by a former excision for biopsy; this contained a few small nodules.

The nodular excrescence was somewhat elastic.[1] On pressure over some parts of the tumor, a rather thin, dirty, sanguineous, puslike fluid, containing many yellowish-white grains the size of a pinhead, appeared out of minute fistulous openings at the top or between the nodules. The sulphur granules were cheese-like in consistency and appearance, and could easily be rubbed down; the grain was then seen to consist of a meshwork of many thin, filamentous, nonsegmented threads, with a diameter of less than 1 micron.

Microscopic Examination.—The histologic picture indicated typical mycetoma. The cutis and principally the corium showed many well defined infiltrates the size of a pea or smaller; at many places these became abscesses. In the middle of most of the abscesses the fungus mass could be observed, the contour of which was irregular. The filaments were gram-negative; they stained blue with Nicolle's carbol-thionine, and pinkish violet with hematoxylin-eosin. At the periphery of the grain, only after staining with Ziehl-Neelsen stain, could one

* Submitted for publication, Sept. 18, 1929.

1. Scheube, B.: Die Krankheiten der warmen Länder, Jena, Gustav Fischer, 1910, p. 1005.

Fig. 1.—Appearance of the diseased foot. The photograph does not show clearly the hyperpigmentation around the nodular mass.

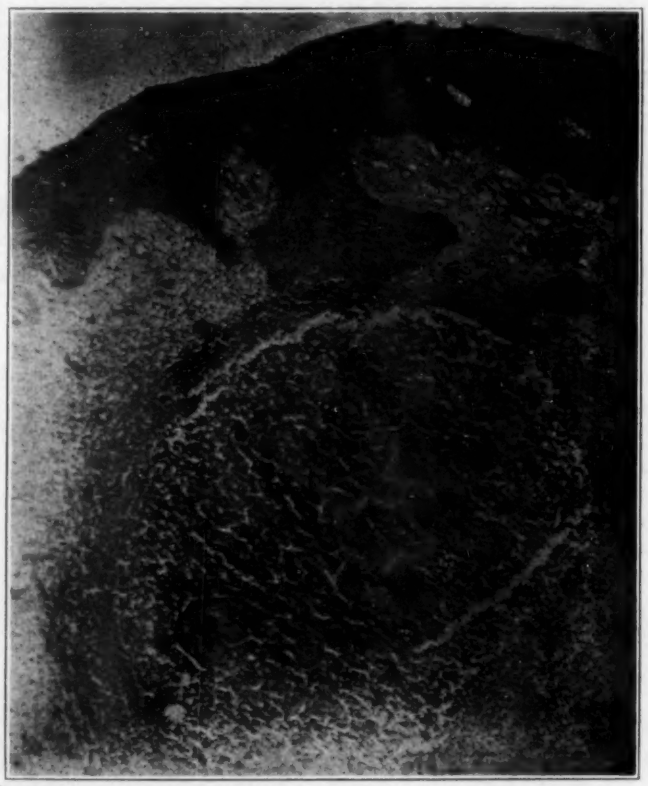

Fig. 2.—Typical structure of mycetoma. Gram stain; low power.

observe an amorphous, deeper colored zone, which was probably identical with the one that Vincent described.[2] In most cases the mycelial mass was surrounded by pus corpuscles and polymorphonuclear leukocytes, as well as by fibrin fibers. Then followed several layers like those in common abscesses until a pyogenic membrane was encountered that consisted of fibrin, polymorphonuclear cells and necrotic tissue; in other abscesses, however, there was a capsule consisting chiefly of fibroblasts and old connective tissue fibers. Around the abscesses, reactive changes of the blood vessel apparatus, such as dilatation, endovasculitis, etc., could be observed, together with many plasma cells and epithelioid cells; I found only one giant cell.

The epidermis showed several changes, mainly, however, a pronounced acanthosis. The stratum germinativum was derived from pigment; chromatophores were lacking.

Fig. 3.—A three weeks' culture of the causative fungus on plain agar.

Mycology.—After planting the grains on different mediums, I obtained the following results:

Plain agar: cream-colored culture; abundant growth; central umbilication.

Glycerinated agar: the same growth as on plain agar.

Maltose agar: grayish-white culture; less abundant growth; in old cultures the nutrient medium turned pink.

Potato: cream-colored to white culture, slightly plicated; old cultures did not become pink or orange.

Hay-infusion: abundant growth, downy puff-balls falling to the bottom.

The optimum of growth was secured at 37 C., in aerobic culture.

I inoculated a guinea-pig and a rabbit subcutaneously, but three months' observation showed no positive results. The guinea-pig was inoculated by placing a wooden splinter covered with particles of the culture into an artificially made pocket of the skin, which was then sutured.

2. Brumpt, E.: Précis de parasitologie, Paris, Masson & Cie, 1927, p. 1196.

COMMENT

Though the growth obtained differed somewhat from *Actinomyces madurae* (Vincent, 1894; Lehmann and Neumann[3] in cultural and staining qualities), I think this fungus has to be considered the cause of this mycetoma.

It seems that the disease is rare in the Dutch colonies. One can read in the well known handbook of Plehn and Mense:[4] "In Niederländisch-Indien scheint es bis jetzt zu fehlen." (In the Dutch Indies it still appears to be absent.) This is nearly true; only one atypical case of mycetoma pedis has been mentioned by Flu.[5]

To my knowledge, any previous occurrence of the disease in Dutch Guiana has not been reported. South American cases of madura foot, however, have been observed in Brazil (Lindenberg, da Silva, Horta, Yazbek), Argentine (Sommer y Greco, Solari), Chile, Nicaragua, Peru (Escomel), Cuba (Desvernine and Albertini), Costa Rica, Panama (Burres), Mexico (Boyd and Crutchfield), Trinidad (Seheult) and French Guiana (Grall and Grand Moursel).

Only a few of the cases reported, however, were caused by *Actinomyces madurae* (Sommer y Grego's, Desvernine and Albertini's and probably the present case).

It is remarkable that the disease occurs rarely in Dutch Guiana, where agriculture is practiced widely and where lesions of the lower extremities are often encountered. Many authors have stated that the occurrence of madura foot is rare in South America; Seheult,[6] who reported a case with black grains, saw this disease only once in twenty-two years of hospital practice.

As the patient in the present case refused operation, I tried to influence the process by administration of heavy doses of potassium iodide and local dressings of compound solution of iodine, without results, however. Acriflavine administered intravenously diminished the suppuration, perhaps by action on the secondary pyogenic invaders. Unfortunately, the patient had to be dismissed uncured at her request.

SUMMARY

A case of mycetoma pedis with yellowish-white grains is reported in a British Indian woman, aged 41, an agricultural laborer, born in Dutch Guiana. Previous occurrence of the disease in Dutch Guiana has

3. Bergey, D. H.: Bergey's Manual of Determinative Bacteriology, London, Baillière, Tindall & Cox, 1926, p. 353.

4. Plehn, A., and Mense, Jr., K.: Das Mycetoma: Handbuch der Tropenkrankheiten, Leipsic, Johann Ambrosius Barth, 1924, vol. 2, p. 663.

5. Flu, P. C.: Een atypisch Geval van Mycetoma Pedis, Geneesk. Tijdschr. v. Nederl.-Indië. **52**:703, 1912.

6. Seheult, R.: Madura Foot in Trinidad, J. Trop. Med. **19**:91 (April 15) 1916.

not been recorded. *Actinomyces, Streptothrix,* or *Nocardia madurae* (Vincent, 1894) was probably the causative fungus in this case, though the growth obtained showed slight differences in cultural and staining properties. Subcutaneous inoculations proved to be unsuccessful. The histologic picture was that of a typical mycetoma, the fungus having given rise mainly to the formation of multiple abscesses in the cutis and of acanthotic alterations of the epidermis. A giant cell could be seen in only one of many preparations. Roentgen examination showed that the bones were not involved, which is a common observation in mycetoma vincentii. Though heavy doses of potassium iodide (up to 7 Gm. a day) were tried, the process did not react favorably.

LICHEN SCLEROSUS ET ATROPHICUS (HALLOPEAU) AND RELATED CUTANEOUS ATROPHIES *

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Atrophies of the skin occupy an important position in dermatology, not because of their rarity, but because of their relation to other diseases of the skin. Lichen sclerosus et atrophicus (Hallopeau) is unique in this way, being assigned a position midway between lichen planus and circumscribed scleroderma (white-spot disease).

Hallopeau [1] described a clinical picture which is unequivocal, but he named his distinct clinical entity "lichen plan atrophique," thereby leaving the way open to much misunderstanding. Darier,[2] who studied the pathologic process in Hallopeau's first case, tried to reconcile the histologic picture he found to that of ordinary lichen planus. He did this by assuming that the original infiltrate, so characteristic of lichen planus, had disappeared, leaving behind sclerosus and atrophy. In the light of the pathologic studies of other workers his assumption does not appear to have been valid. Darier also suggested that the term sclerosus might be used on the basis of the pathogenesis, and the term atrophicus on the grounds of the clinical appearance. He was the first to suggest the complete name by which the condition is now commonly known.

Cases similar to Hallopeau's soon were reported under various names by other continental writers. Most of these writers were inclined to place their cases in the circumscribed scleroderma group of disorders of the skin. They likened them to the "Kartenblattähnlich" scleroderma of Unna.[3] The basis of their grouping was primarily on the histologic similarities of these conditions. So there are two opinions as to the classification, the original one of Hallopeau, seconded by Darier, placing it in the group of atrophic lichen planus, and the later ones placing similar conditions with the circumscribed sclerodermas.

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* Submitted for publication, Aug. 28, 1929.

1. Hallopeau, H.: Leçons clinique sur les maladies cutanées et syphilitiques, Union méd. **43**:742 (May) 1887; abstr., Ann. de dermat. et syph., vol. 8, p. 790, under the title "Du lichen plan et particulier de sa forme atrophique."

2. Darier, J., in discussion on Hallopeau, H.: Union méd. **43**:742 (May) 1887.

3. Unna, P. G.: Kartenblattähnliche Sclerodermie in Die Histopathologie der Hautkrankheiten, Berlin, A. Hirschwald, 1894, p. 1121; English translation by Norman Walker, New York, The Macmillan Company, 1896, p. 1103.

A translation of the summary given by Hallopeau in his original article gives a complete clinical picture:

Lichen planus atrophicus begins by papules as in ordinary lichen planus. The papules are pruriginous but are much paler in color though morphologically similar. As they grow older they become still paler and then efface themselves, leaving white areas with a cicatricial appearance which are remarkable by the presence of punctiform depressions. The eruptive elements group themselves and become confluent, forming plaques several centimeters in diameter whose surface is "quadrillée et criblée de dépressions ponctiformes." The contours of the plaques are irregular. At the periphery are newer lesions, some decolorized, others still slightly reddened and active. The eruption appears in successive attacks.

He then differentiated the condition he described from morphea and from ordinary lichen planus.

Darier studied the histologic aspects of Hallopeau's first case. He found that there was an increase in the stratum corneum and stratum granulosum. This hyperkeratosis was most marked at the orifices of the sweat ducts and the hair follicles, where plugs were formed. The stratum mucosum was markedly atrophied, and the rete pegs were absent. The border between the epidermis and cutis was only a wavy line. The papillary bodies had disappeared. The connective tissue of the upper epidermis was felted and homogenized. Here the elastic tissue had disappeared except for a few remnants where the papillae had been. There was also sclerosis of the connective tissue of the deeper cutis, and it was here that the mild inflammatory reaction occurred. This was evidenced by a perivascular infiltrate consisting chiefly of round cells involving some of the deeper blood vessels. There was no effect on the vessel walls nor on their intima. Because the biopsy was taken from a relatively old lesion he assumed that the original infiltrate had disappeared, leaving behind atrophy of the epidermis, sclerosis of the subpapillary connective tissue and remnants of infiltrate about some of the vessels of the deeper cutis.

In the past year I have had an opportunity to observe a patient with typical lichen sclerosus et atrophicus (Hallopeau), another with an atrophy corresponding to Unna's cardlike scleroderma and a third with ordinary lichen planus followed by large areas of atrophy. Sections of biopsies from these three cases have been studied and compared. The clinical histories and observations are given in the following case reports.

REPORT OF CASES

CASE 1.—*Lichen Sclerosus et Atrophicus (Hallopeau).*—An obese woman, aged 69, had had an itching eruption on the skin for ten years. It began as an itching white spot over the left clavicle; then itching patches appeared on the opposite clavicle, on both trapezius ridges and on the back. From then to the present the condition slowly spread by the appearance of new lesions in the areas adjacent to the older ones, usually with subsequent coalescence. The lesions in

various stages of development were limited to the body. They were present on the back of the neck, where they extended up into the scalp as high as the occipital protuberance. Over the shoulders, scapular region, clavicles and upper part of the chest, the smaller lesions had fused into large, atrophic, circinate outlined patches. Between these areas there was normal though hyperpigmented skin. Even in the large patches, entirely surrounded by atrophic skin, were seen small islets of normal skin. Over the breasts and at the costal margin there were

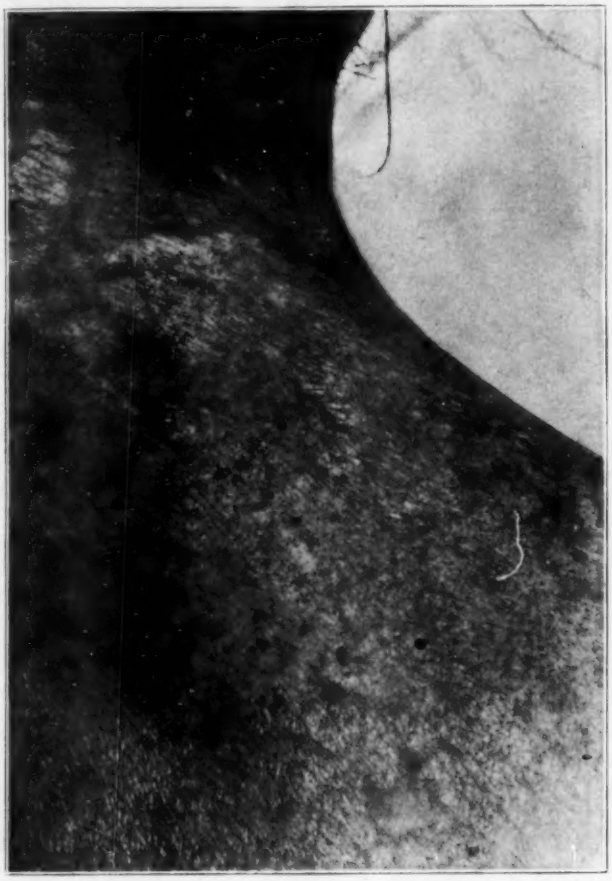

Fig. 1 (case 1).—Close-up of the oldest lesions over the right scapular region. Of especial note are: the marked comedone-like plugging, the extensive parchment-like atrophy, the lesions extending beyond the hair line and the hyperpigmentation of the normal skin.

smaller scattered areas of atrophy. The most recent lesions, of a few weeks' duration, were present over the lower part of the sternum. In the sacral region was a slightly older patch of lesions, which were still in the papular stage.

The best conception of this disorder can be gained by a description of the lesions present, which are in all stages of development and atrophy.

The youngest lesions, present for only a few weeks, were located over the lower end of the sternum. The lesions here were small, mother-of-pearl white, polygonal, cleancut, definitely elevated papules. They were the size of a large pinhead, being from 1.5 to 2.5 mm. across. Each papule was separated from the adjacent one by an area of normal skin several millimeters across. The entire patch was about 5 cm. in diameter and consisted of many dozens of papules. There was no suggestion of a red color nor of a red areola in the papules, even the smallest papules being ivory colored and clearcut.

The next older lesions, which were about six months old, were grouped in a larger patch over the sacral region. The papules still retained their elevation and polygonal outline. They were larger, being from 3 to 5 mm. wide. In the center of the patch, the papules bordered on each other, making an appearance like that of a depigmented lichen simplex chronicus. At the borders the papules were still discrete. They were of the same whitish hue, but there was still no ocular evidence of atrophy.

The remainder of the eruption was in the atrophic stage and consisted of lesions which varied from 5 mm. for the smaller isolated lesions to 12 cm. or more for the irregular atrophic patches over the shoulders, scapulae and clavicles. These were essentially the same except for size. The characteristics were best seen in the smaller atrophic lesions. These were slightly depressed and of a parchment-like color and consistency. They showed a fine wrinkling and an exaggeration of the normal lines of the skin. With the aid of a hand lens small depressions could be seen on the surface at the orifices of the sweat ducts and hair follicles. In the very old, large, atrophic areas in the suprascapular region there was formation of the comedone-like plugs which are so characteristic of the late atrophic stage. Here the skin had a rough sandpaper-like feel, but there was little if any binding down of the skin. There were no lesions in the mouth.

Aside from the skin trouble, the patient had had no serious illness. She was slightly nervous but considered herself in good health. She weighed 172½ pounds (78.3 Kg.); her height was 61½ inches (154 cm.). The temperature was 97.6 F., and the pulse rate 104. The blood pressure was 180 systolic and 105 diastolic. The thyroid gland was slightly enlarged, the right lobe more so than the left. Examination of the chest and heart showed a soft, blowing, systolic murmur at the apex of the heart, which was not enlarged. She had beginning senile cataracts of both eyes. Aside from this, a thorough general examination revealed nothing.

Urinalysis showed a moderate trace of albumin but no sugar or casts. As an uncatheterized specimen was used, it was not considered significant. An examination of the blood showed a hemoglobin of 85 per cent, a red corpuscle count of 4,880,000 and a white corpuscle count of 7,600. A determination of the basal metabolic rate gave a reading of + 28 which was above the upper limits of normal.

To study the pathologic changes, two pieces of skin were removed. One, from the sacral region, was taken when the lesions were only a few weeks old and still in the papular stage. The other was taken from the scapular region where the eruption had been present for years and showed the characteristic plugging.

Examination of the section taken from the sacrum when the lesions were still in the papular stage, and not very old, showed, even in this stage, rather marked atrophy of the prickle cell layer. There was also moderate hyperkeratosis which was most noticeable at the hair follicles where there were horny plugs at the mouths of the follicles. The rete ridges, as well as the papillary bodies, had flattened out. The greatest change was in the connective tissue of the papillary and subpapillary regions, where it was finely fibrillar and rather loosely felted.

Toward the edge this zone of early sclerosis was narrow, extending only a short distance beneath the surface epidermis. Toward the center of a papule the sclerosis extended down farther, almost reaching the level of the sweat glands. The elastic tissue was completely absent in the sclerotic zone. Beneath it the elastica was moderately well preserved, showing only slight fragmentation. There was no cellular infiltrate in the sclerotic zone of the papillary region. Just beneath the atrophic epidermis there were a few spaces formed apparently by dilated lymphatics.

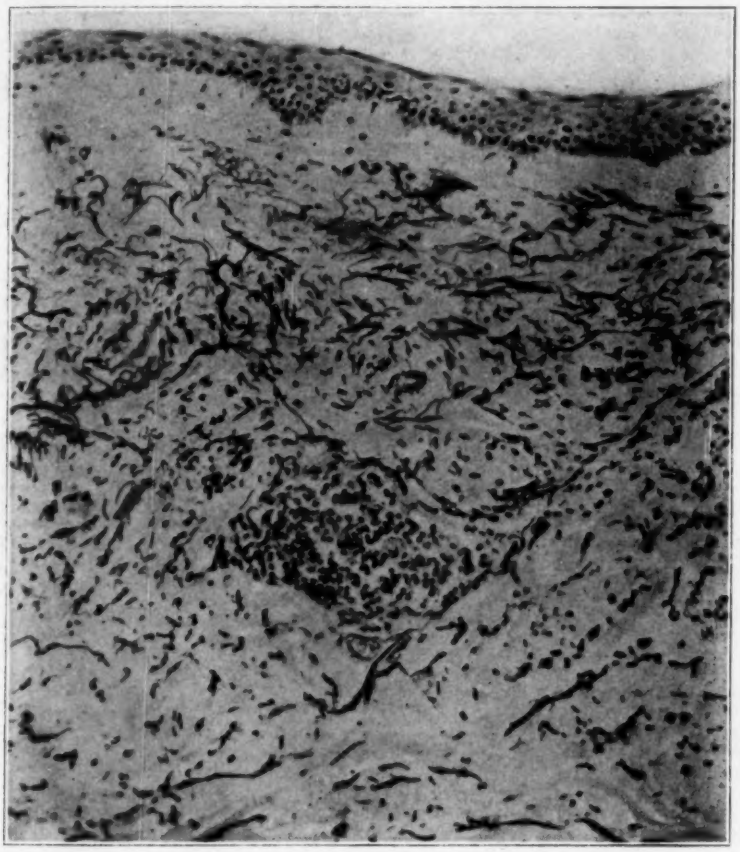

Fig. 2 (case 1).—Section from the edge of a fairly young papule from the sacral region. The section shows: atrophy of the epidemis, a narrow band of sclerosis with complete disappearance of the elastic fibers in the papillary region, some thickening and fragmentation of the deeper elastic fibers and an area of round cell infiltrate about a blood vessel of the deeper cutis. Hematoxylin-acid orcein stain.

At the border of the sclerosed connective tissue there were a few small collections of round cells; some of these were perivascular while others were independent of the vessels. The sweat glands showed a moderate cystlike dilatation of a few of the tubules; otherwise they were fairly normal.

Biopsy of the section from the scapular region showed only a more advanced stage of the same process. The atrophy of the epidermis was more marked, the sclerosis of the papillary and subpapillary connective tissue was greater, the follicular plugs were larger, the cell infiltrate beneath the sclerotic connective tissue was less marked and the sweat glands showed more atrophy.

Fig. 3 (case 1).—Section from the center of the same papule as in figure 2. The pathologic process is essentially the same as in figure 2, but the sclerotic band is wider and the atrophy of the epidermis more marked. The edge of a follicular plug can be seen in the upper right corner. Hematoxylin-acid orcein stain.

The pathologic observations agree with those of practically all the cases reported. Darier,[4] in a subsequent report on the pathologic changes in lichen sclerosus et atrophicus (Hallopeau), compared the

4. Darier, J.: Lichen plan scléreux, Ann. de dermat. et syph. **3**:833, 1892.

cell infiltrate to that of ordinary lichen planus. The difference is that in ordinary lichen planus the infiltrate is immediately beneath the epidermis, while in lichen sclerosus et atrophicus (Hallopeau) it is beneath the sclerotic zone which is immediately below the epidermis. Ormsby,[5] in his paper, agreed with Darier. Schamberg[6] did not think that the pathologic process in his case was like that of lichen planus. Alexander[7] thought that there was some resemblance between the pathologic process in lichen planus and that in lichen sclerosus et atrophicus (Hallopeau). Fischer,[8] Bizzozero[9] and Kreibich[10] thought that microscopically lichen sclerosus et atrophicus (Hallopeau) resembled the circumscribed sclerodermis, particularly Unna's card-like scleroderma, rather than lichen planus.

In none of the cases reported was there a diffuse, sharply limited round cell infiltrate of the papillary and subpapillary layers, as in classic lichen planus. The subpapillary region was always the site of sclerosis of the connective tissue with a moderate cell infiltrate beneath. As will be shown in the third case of this series, moderate remnants of the cell infiltrate of lichen planus are present in the papillary and subpapillary regions when the epidermis shows marked atrophy. If an infiltrate of the papillary and subpapillary layers similar to that of ordinary lichen planus is present in lichen sclerosus et atrophicus (Hallopeau), it must disappear as soon as the sclerosis begins, leaving remnants only beneath the sclerotic layer. This is the essence of Darier's[4] explanation of the pathogenesis.

No treatment that the patient received was of any avail. Her condition had been steadily progressive since the onset. In 1927, a prolonged course of treatment with corrosive mercuric chloride, given intramuscularly, was without effect. Later she was given a series of injections of sodium thiosulphate intravenously without improvement. In 1928, a series of roentgen treatments of the spine, after the method of Gouin,[11] was given without success. The most effective method of controlling the pruritus had been by fractional doses of the roentgen rays given to the affected places. The amount given had been one-fourth

5. Ormsby, O. S.: Lichen Planus Sclerosus et Atrophicus (Hallopeau): A Report of Six Cases (Five New) with a Review of the Literature, J. A. M. A. **55**:901 (Sept. 10) 1910.

6. Schamberg, J. F., and Hirschler, Rose: Lichen Sclerosus et Atrophicus: With Report of a Case, J. A. M. A. **53**:369 (July 31) 1909.

7. Alexander, Arthur: Der Lichen Sclerosus, Arch. f. Dermat. u. Syph. **121**:925, 1916.

8. Fischer, W.: Ueber eine dem Lichen Sclerosus (Hallopeau) angenäherte form der zircumskripten Sklerodermie, Arch. f. Dermat. u. Syph. **110**:159, 1911.

9. Bizzozero, Enzo: Ueber die Sklerodermia circumscripta und ihre Beziehungen zum Lichen Sclerosus, Dermat. Ztschr. **22**:517, 1915.

10. Kreibich, C.: Lichen Sclerosus, Arch. f. Dermat. u. Syph. **124**:587, 1915.

11. Gouin, J., bibliography of Driver, J. P.: Roentgen-Ray Treatment of the Spine in Lichen Planus, Arch. Dermat. & Syph. **19**:620 (April) 1929.

erythema dose measured according to the indirect method of MacKee.[12] The treatments were given infrequently as the symptoms warranted, not oftener than every three weeks.

This typical case of lichen sclerosus et atrophicus (Hallopeau) is unusual in several ways. The prolonged duration, ten years, during which time the patient has scarcely ever been free from newly developed lesions, is extraordinary. The extent of the eruption is greater than in any case that has been encountered. The presence of lesions in the scalp is remarkable. In none of the cases met with has this been previously noted and reported.

Following Hallopeau, cases in which an atrophy is an outstanding feature have been reported. Among these the more important are, lichen albus (Zumbusch[13]) and chronic atrophic lichenoid dermatitis (Csillag[14]), which approach lichen sclerosus et atrophicus (Hallopeau) in their clinical and pathologic appearance. Cardlike scleroderma, white-spot disease and scleroderma guttata form a group clinically and pathologically almost, if not quite, identical with each other. Clinically, they are different from lichen sclerosus et atrophicus (Hallopeau), resembling it only pathologically. Their classification has now been fairly well determined by many writers. Ordinary lichen planus with atrophy is distinctive, both clinically and pathologically. It always enters into the discussion probably because Hallopeau originally designated his case as lichen planus atrophicus. Hallopeau's[15] later case reports served to establish the condition he described as a clinical entity, but he did not settle the nosologic position of the disorder.

Ormsby[5] clearly distinguished the three groups mentioned, emphasizing their similarities and their differences, chiefly on clinical grounds, but also on histologic variations. He considered that lichen sclerosus et atrophicus (Hallopeau) was related to lichen planus. He pointed the way to the simplification of the grouping of these rare disorders and reviewed most of the cases then reported.

To attempt to classify accurately many of the cases similar to lichen sclerosus et atrophicus (Hallopeau) that have been reported under various names would be futile. Many writers have tried but they have not come to the same conclusions. Hallopeau[16] thought that lichen

12. MacKee, G. M.: X-Rays and Radium in the Treatment of Diseases of the Skin, ed. 2, Philadelphia, Lea & Febiger, 1927, chaps. 18 and 19.

13. Von Zumbusch, Leo Ritter: Ueber Lichen Albus, eine bisher unbeschriebene Erkrankung, Arch. f. Dermat. u. Syph. **82**:340, 1906.

14. Csillag, Jakob: Dermatitis lichenoides chronica atrophicans (Lichen Albus v. Zumbusch), Ikonographia Dermat. Fasc. **4**:147, 1909.

15. Hallopeau, H.: Lichen plan scléreux, Ann. de dermat. et syph. **10**:447, 1889; Sur un nouveau cas de lichen plan atrophique, ibid. **7**:57, 1896; Sur un nouveau cas de lichen de Wilson scléreux, ibid. **9**:359, 1898.

16. Hallopeau, H.: Sur la nature du lichen blanc de von Zumbusch, Bull. Soc. franç. de dermat. et syph. **18**:107, 1907.

albus (Zumbusch) was the same condition that he had described. Bizzozero [9] thought that lichen albus was a transitional form which approached Unna's cardlike scleroderma. He thought that lichen sclerosus et atrophicus (Hallopeau) was separate from lichen planus and from circumscribed scleroderma, but he confuses the reader by too many transitional groupings and subgroupings. Alexander [7] thought that lichen albus was closely related to circumscribed scleroderma, but that his cases were similar to Hallopeau's and thus related to lichen planus. Fischer [8] reported a case which he classified with lichen albus that he thought should be grouped with circumscribed scleroderma rather than with lichen planus. The basis of his classification rested on the pathologic similarities of lichen albus to circumscribed scleroderma. Csillag,[14] in reporting his case, considered it the second case of lichen albus, but he objected to the name because he did not think that lichen albus was related to lichen planus. He thought that chronic atrophic lichen dermatitis was a better name.

Wise and Shelmire [17] recently reported two cases of chronic atrophic lichenoid dermatitis (Csillag) in which they pointed out the similarity of this condition to lichen sclerosus et atrophicus both clinically and histologically. They concluded from the clinical standpoint that neither of their two cases could be properly grouped with lichen planus sclerosus, white-spot disease or scleroderma. Ormsby, who observed one of the cases reported, was not certain but that the condition might be lichen atrophicus et sclerosus. He was, however, agreeable to the classification as a separate entity.

To go further would be needlessly confusing. To the average medical reader, lichen sclerosus et atrophicus (Hallopeau), lichen albus (Zumbusch) and chronic atrophic lichenoid dermatitis (Csillag) appear similar. Clinically, they all begin as elevated, achromatic, usually polygonal papules which later show parchment-like atrophy and confluence of the lesions into larger patches. Pathologically, they all show atrophy of the epidermis, sclerosis of the layers immediately under the epidermis and slight inflammatory reaction beneath the zone of sclerosis.

The second case of this group was presented by Oliver and Finnerud [18] before the Chicago Dermatological Society with a provisional diagnosis of lichen sclerosus et atrophicus. At that time Ormsby thought that the case was more than likely a circumscribed scleroderma (Unna's cardlike scleroderma). Further observation during a period of several months convinces me that the patient should be placed in the latter group. Her history is given in case 2.

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17. Wise, F., and Shelmire, B.: Chronic Atrophic Lichenoid Dermatitis (Csillag): So-Called Lichen Albus of Zumbusch, Arch. Dermat. & Syph. **18**:179 (Aug.) 1928.

18. Oliver, E. A., and Finnerud, C. W.: Lichen Planus Sclerosus et Atrophicus, Arch. Dermat. & Syph. **19**:829 (May) 1929.

CASE 2.—*Circumscribed Scleroderma (Cardlike Scleroderma).*—The patient was an obese, though healthy, single woman, aged 26, whose skin condition began about eighteen months before she was first seen. When she first noted the eruption it consisted of several small white spots on the right side of the neck behind and below the ear. She did not remember any subjective symptoms at the beginning. The initial white spots grew larger and coalesced to form a patch about 2.5 cm. in diameter. Shortly thereafter another group of white spots appeared below the original patch. They developed similarly. Since the onset both patches had enlarged, she thought both by peripheral extension of the margin

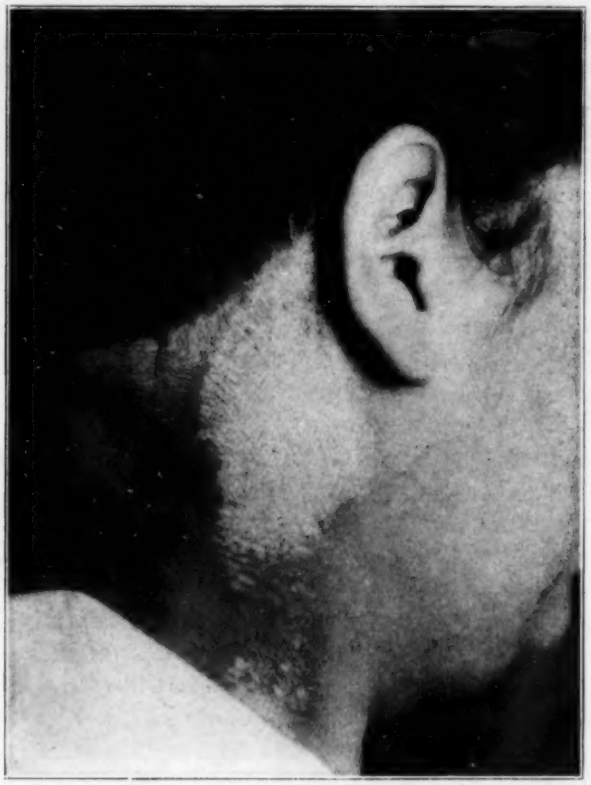

Fig. 4 (case 2).—The older patch and the upper part of the newer patch with smaller lesions between. Of note are: the marked follicular plugging, the rather sharp limitation of the upper patch and the extension of the upper patch into the scalp.

and by the appearance of new white spots beyond the edge which enlarged and later fused with the larger patches. For a while the process seemingly was arrested, but in the past few months, while she had been under observation, new small atrophic lesions had appeared between the two large old ones. There was a slight subjective sensation of tautness with drawing in the larger lesions. She complained of a mild pruritus.

The eruption was limited to the right side of the neck and consisted of two large patches with small satellite lesions between them. The upper patch was

about 7.5 by 6 cm. Its upper border extended a short distance into the scalp. It was porcelain white, had a rather firm, bound-down consistency, and was thickly studded with comedone-like plugs which gave it a sandpaper-like sensation to the touch. The upper, anterior and posterior borders were fairly definitely defined. The lower border was not as distinct and had the satellite lesions previously mentioned. The newer, smaller patch had its center several inches below. Its borders were not as regular nor as clearcut. It did not have the porcelain white of the older patch, and it lacked the marked comedone-like plugging. It was much less firm in consistency than the older patch and had a parchment-like fine

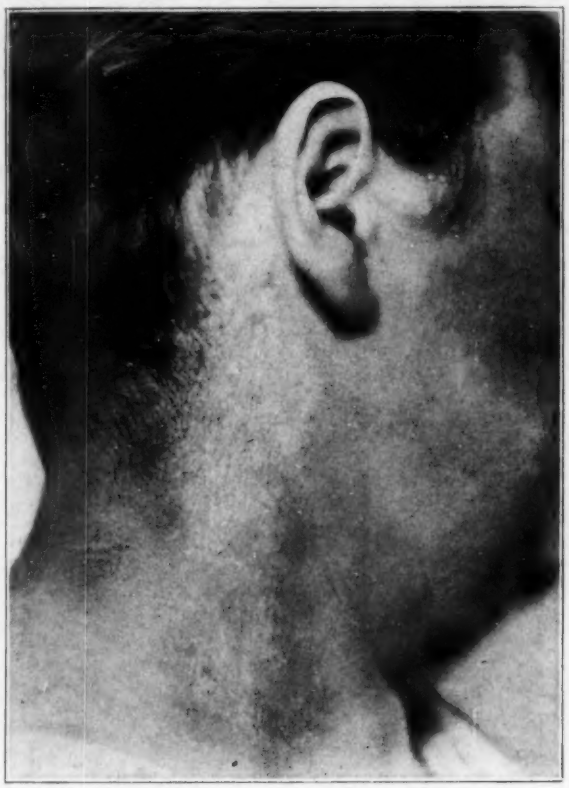

Fig. 5 (case 2).—Picture taken about eight months after the patient was first seen. It shows the extent of healing of both lesions.

wrinkling and atrophy. The new, small, elementary lesions were most numerous between the two patches. The earliest lesions consisted of nonelevated, white spots, the size of a pinhead, which slowly enlarged to the size of a pea or larger. They then fused, either with adjacent spots or with one of the larger lesions. The small elementary lesions were never elevated or papular, were always flat, had the same consistency as the adjacent skin and from the beginning were achromatic with no red or violaceous halo. Atrophy was evident macroscopically even in the smaller lesions. There was hyperpigmentation of the surrounding skin, but this might possibly have been due to the "sunlight" treatments which the patient received elsewhere.

The past history was of no significance. A physical examination showed nothing but a rather marked obesity. The patient was 62 inches (155 cm.) tall and weighed 205 pounds (93.2 Kg.). The blood pressure was 110 systolic and 80 diastolic. The urine was normal, and a complete blood count showed nothing abnormal. A determination of the basal metabolic rate gave a reading of —10. A diagnosis of endogenous obesity was made. In regard to the obesity the family history may be of significance in that the patient's father was obese, and that all his sisters were supposed to have diabetes. Her mother was not obese.

A biopsy was made from the border of the old comedone-like, studded patch before any treatment was given. The sections showed a relative hyperkeratosis

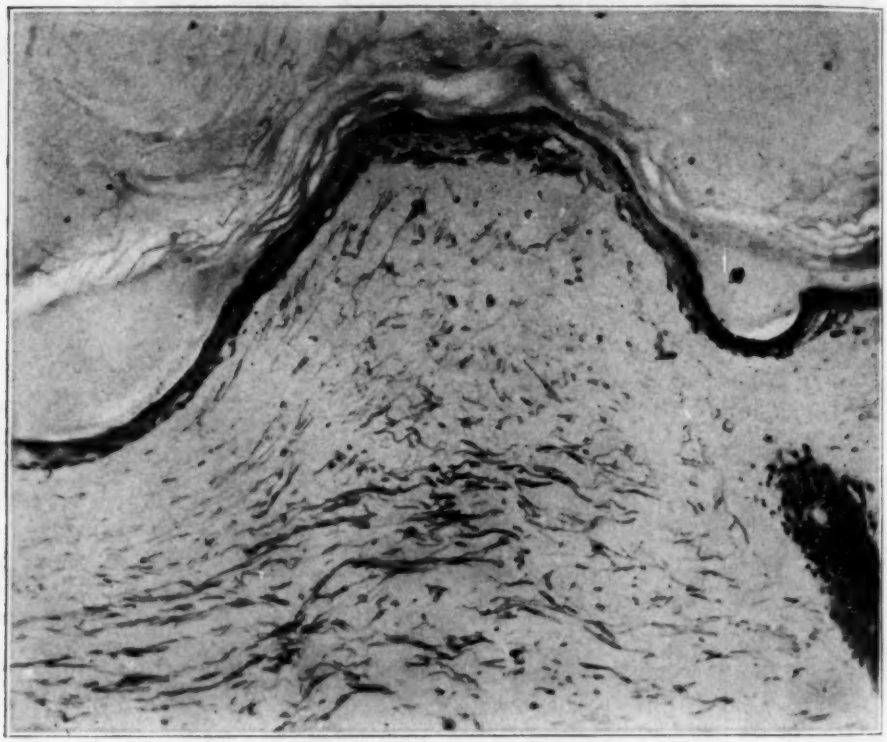

Fig. 6 (case 2).—Section from near the edge of the old patch near the ear. It shows the follicular hyperkeratosis and marked atrophy of the epidermis. The elastic tissue has largely disappeared from the sclerotic subepithelial region, but remnants still remain. There is no inflammatory reaction in this section. Note the similarity of the pathologic process to that of lichen sclerosus et atrophicus, figure 3, case 1. Hematoxylin-acid orcein stain.

of the stratum corneum with marked plugging of the follicular orifices. There was far advanced atrophy of the stratum mucosum which consisted of from two to four layers of horizontally elongated cells. The rete pegs and the papillary bodies were entirely flattened out. The papillary and subpapillary connective tissue was sclerotic and homogenized. The elastic tissue had disappeared from

this region. There was no cell infiltrate in this sclerotic area. There was some atrophy of the sweat glands with occasional dilatation of the ducts. Beneath the sclerotic area there was moderate infiltration of round cells about some of the vessels and the adnexa of the skin. The disklike area of sclerosis described by Unna [3] and other writers was not found, probably because the biopsy was taken from an old portion of the lesion. The pathologic changes corresponded fairly well with the second case described by Unna.

The treatment instituted consisted of restriction of the diet and internal administration of desiccated thyroid gland in doses of 1 grain (0.06 Gm.) three times daily. Under this regimen the weight was reduced 22 pounds (10 Kg.) in four months. Locally, the roentgen rays in dosages of one-fourth unit (MacKee) were given for a total of eight treatments. This caused a decrease in the consistency and a smoothening of the comedone-like plugging of the older lesion, but it did not have any effect on the development of new lesions. The new elementary lesions, which have been described, appeared in greatest number about two months after the roentgen treatments were discontinued.

In the past few months there had been great improvement on thyroid therapy alone. The newer lesions had ceased to appear and the older ones were much better. The lower patch had almost disappeared, only a few white areas remaining. The older sclerotic patch was 50 per cent improved. The healing was evidenced as a return of pigmentation which began at the edge and worked toward the center; a few atrophic places were still present. The healed areas presented no gross abnormalities except hyperpigmentation. No atrophy was evident to the eye or the palpating finger. Whether this improvement was incidental or a result of the treatment is problematic. The patient lost no more weight and had no toxic symptoms from the ingestion of desiccated thyroid.

This case is almost a duplicate of a case that Milian [19] described, but, according to Darier, is misnamed. In his case there was also marked plugging of the follicular openings, which is considered unusual in this form of circumscribed scleroderma. Riecke [20] also reported a case in which comedo-like plugging was present. More recently, Grutz [21] described a case of circumscribed scleroderma with extensive plugging in the atrophic patches. He thought that it differed from cardlike scleroderma only in that follicular, comedo-like plugs were present.

In lichen sclerosus et atrophicus (Hallopeau) much attention was formerly placed on the presence of the comedo-like plugging. This overemphasis of follicular plugging as an important diagnostic point has undoubtedly caused considerable difficulty. Certain forms of lichen planus, lichen planopilaris,[22] have follicular plugging. Senear and

19. Milian, G.: Lichen plan atrophique ou mieux leucodermie atrophique ponctuée, Discussion by Darier, Bull. Soc. franç. de dermat. et syph. **20**:279, 1909.

20. Riecke, E. P.: Zur Kenntnis der Weissfleckenkrankheit (White-Spot Disease), Arch. f. Dermat. u. Syph. **99**:181, 1910.

21. Grutz, O.: Sclerodermia guttata follicularis, Dermat. Ztschr. **53**:227, 1928.

22. Ormsby, O. S.: Lichen Planopilaris (Pringle), in Treatise on Diseases of the Skin, ed. 3, Philadelphia, Lea & Febiger, 1927, p. 305. Nomland, R.: Lichen Planopilaris, Arch. Dermat. & Syph. **19**:830 (May) 1929.

Wien [23] recently showed a case of lichen planus with a large area of atrophy in which follicular plugging was present.

The extensive review of MacKee and Wise,[24] and the papers of Montgomery and Ormsby [25] and of others have definitely decided the nosologic position of "white-spot disease" as a form of circumscribed scleroderma. Unna gave the name "Kartenblattähnlich" scleroderma to a condition characterized by the presence of mother-of-pearl or chalky white patches of atrophy. According to him, the essential pathologic process was a plate or disklike sclerosis of the papillary and subpapillary connective tissue with disappearance of the elastica. At the border of the area of sclerosis there was a moderate round cell infiltrate, mostly independent of the blood vessels. He considered the atrophy of the epidermis as incidental to the sclerosis. Cardlike scleroderma formed one of three varieties of circumscribed scleroderma, the other two being the keloid-like and morphea.

Dreuw [26] reviewed the literature and considered that white-spot disease and cardlike scleroderma were the same. Kretzmer [27] was of the same opinion. In general, most continental writers consider that white-spot disease and cardlike scleroderma are identical varieties of circumscribed scleroderma. Kyrle,[28] however, thought that white-spot disease was different histologically from morphea. Gans,[29] on the other hand, described it as similar to the other varieties of circumscribed scleroderma.

The third case of this group represents an unusual manifestation of a not uncommon skin disease. Ordinary lichen planus with atrophy is well known; the patient whose case is reported showed several unusual manifestations of the disease. He was twice presented before the Chicago Dermatological Society [30] at intervals of about a year. His history is given in case 3.

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23. Senear, F. E., and Wien, M. S.: Report of Case, Meeting of Chicago Dermatological Society, April 17, 1929.

24. MacKee, G. M., and Wise, F.: White Spot Disease, J. Cutan. Dis. **32**:629, 1914.

25. Montgomery and Ormsby, O. S.: White Spot Disease and Lichen Planus Sclerosus et Atrophicus, J. Cutan. Dis. **25**:1, 1907.

26. Dreuw: White Spot Disease or Sclerodermia Circumscripta, Dermat. Stud. **21**:214, 1910.

27. Kretzmer, E.: Zwei Fälle von multipler Kleinfleckeger Sclerodermia circumscripta (White-Spot Disease), Arch. f. Dermat. u. Syph. **118**:148, 1913.

28. Kyrle, Joseph: Vorlesungen über Histo-Biologie der Menschlichen Haut und ihrer Erkrankungen, Berlin, Julius Springer, 1925, vol. 1, p. 140.

29. Gans, Oscar: Histologie der Haut Krankheiten, Berlin, Julius Springer, 1925, vol. 1, pp. 99 and 306.

30. Senear, F. E.: Lichen Planus, Arch. Dermat. & Syph. **19**:143 (Jan.) 1929.

CASE 3.—*Lichen Planus with Atrophy.*—The patient, a well nourished man, aged 42, had an itching skin disease for more than two years. The condition began as small itching spots on the face and body. It had progressed slowly since the onset, both in extent of the eruption and in size of the individual lesion. The larger lesions on the scalp, arms and elsewhere had arisen from the confluence of several smaller lesions.

Except for a mild arthritis and the loss of one leg above the knee as the result of an accident, the past history was of no significance. He had had no venereal diseases.

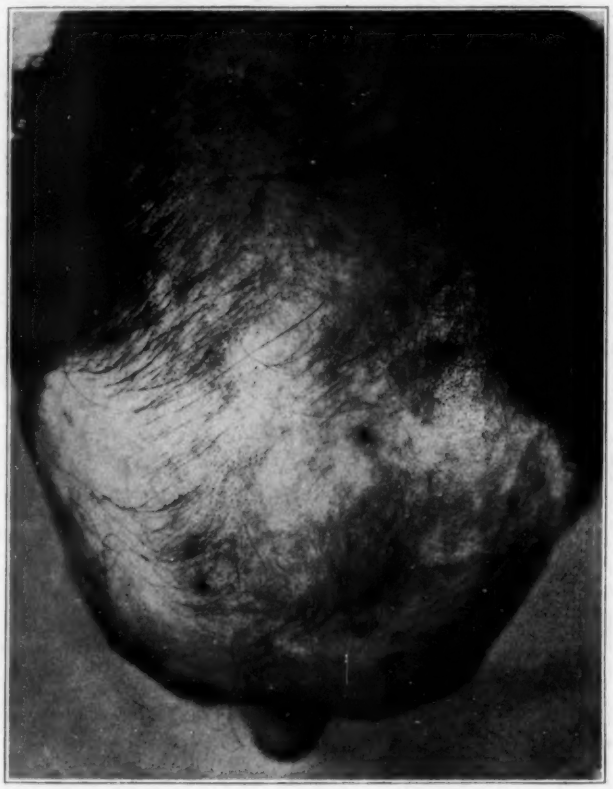

Fig. 7 (case 3).—Scalp which shows the large nonpigmented area of atrophy with permanent complete alopecia.

An examination of the skin revealed a generalized eruption which involved the scalp, face, arms, legs and body. The majority of the lesions were from 0.5 to 1.5 cm. in diameter. They were brown, atrophic, finely wrinkled, depressed macules, many of which had a narrow, elevated, violaceous, shiny margin. There a few flat-topped, small, angular papules still presented. In the mouth there were a few white lines and small white areas. There was a tendency for grouping of the lesions on the flexor aspects of the forearms, on the legs, over the sacral region and in the groin.

The condition of the scalp was unusual. Here there was a large area of atrophy, 5 by 10 cm., which had been formed by the confluence of several smaller lesions. In contradistinction to the lesions on the body there was no pigmentation. The patient had the ordinary presenile type of alopecia, but in the region of atrophy there was complete absence of hair. There was an area of atrophy, 5.5 by 2.5 cm., on the right forearm, as well as some smaller ones in the region of the crest of the ilium, sacrum and sternum; all were formed by the coalescence of the smaller atrophic lesions.

Fig. 8 (case 3).—Back view, showing the extent of the lesions and the grouping and coalescence of the patches over the sacrum.

A biopsy was taken from the edge of the large atrophic place on the forearm. It showed a relative hyperkeratosis of the stratum corneum and a marked atrophy of the prickle cell layer, which in some places was reduced to three layers. The rete pegs and papillary bodies were all flattened out. The papillary and subpapillary regions were still the site of a moderate cell infiltrate. The cells were mostly round cells of the appearance of lymphocytes with a few pigment-bearing cells in the upper cutis. The infiltrate was sharply limited at its lower

margin. The elastic tissue had been largely destroyed by the infiltrate, but remnants of it still remained. The deeper elastic and connective tissue was normal. There was moderate infiltration of round cells about the adnexa of the skin. The cell infiltrate of the upper cutis in this case contrasted sharply with the picture in the other two cases in which no infiltrate was present in the papillary or subpapillary regions. The typical pathologic process of lichen planus was easily recognizable even in this late stage.

A complete general examination was made but nothing of note was found. A Wassermann test and a urinalysis gave negative results.

Fig. 9 (case 3).—Front view, showing the distribution, extent and size of the brown pigmented, atrophic lesions. The coalescence of the lesions near the sternal notch should be noted.

The treatment given was of no avail in preventing either the appearance of new lesions or the enlargement of the old ones. The patient had received a course of several injections of neoarsphenamine elsewhere, on the supposition that the lesions were syphilitic, but with no therapeutic effect. A prolonged course of red mercuric iodide by mouth was without effect, as was also a course of corrosive mercuric chloride given intramuscularly. A series of three roentgen treatments to the spine, given after the method of Gouin, was without beneficial result.

The skin manifestations in the case described are unusual in the wide extent and great number of the atrophic lesions, in the large size of some of the atrophic patches, but particularly in the atrophic lesion followed by complete permanent alopecia in the scalp. This observation is extremely rare; Brocq [31] did not even mention it. In a cursory search of the literature, only Dubreuilh and Petges [32] seem to have given this observation any consideration. They found that ordinary

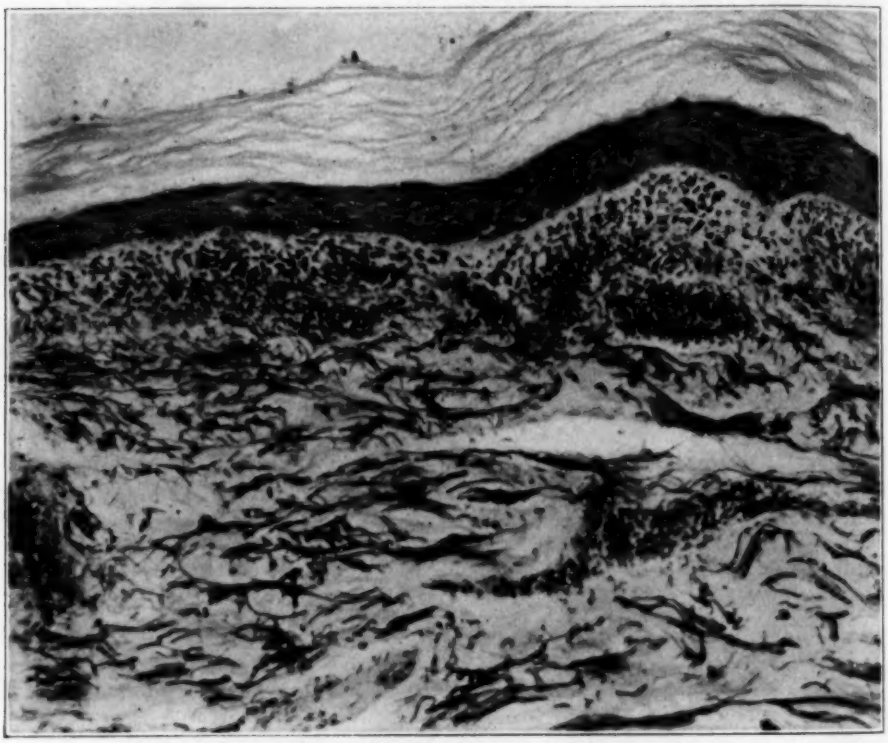

Fig. 10 (case 3).—This section shows rather marked hyperkeratosis and atrophy of the epidermis. A still somewhat dense, sharply limited infiltrate of round cells occupies the upper cutis where the elastic tissue has been destroyed by the inflammatory reaction. There is a moderate round cell infiltrate of the deeper cutis. Hematoxylin-acid orcein stain.

lichen planus may cause permanent atrophic alopeciac patches when it occurs in the scalp.

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31. Brocq: Les lichens, in Besnier, Brocq and Jacquet: La pratique dermatologique, Paris, Masson & Cie, 1900-1904, vol. 3, p. 207.

32. Dubreuilh, W., and Petges, G.: Lichen plan atrophique, Ann. de dermat. et syph. **8**:715, 1907.

That lichen planus with atrophy is distinct from lichen sclerosus et atrophicus (Hallopeau) was shown by Schamberg and also by Ormsby. In the clearcut cases there should be no difficulty in diagnosis, and in the borderline cases a biopsy will give information which will be sufficient to differentiate the two. On the contrary, cardlike scleroderma must be differentiated from lichen sclerosus et atrophicus (Hallopeau) chiefly on clinical grounds, because the pathologic appearances are so similar.

Table of Comparison

	Lichen Sclerosus et Atrophicus (Hallopeau)	Cardlike Scleroderma (Unna)	Lichen Planus with Atrophy
Symptoms	Very mild pruritus	Usually none	Pruritus of varying severity
Elementary lesions	Achromatic, flat-topped, elevated, polygonal papule	Achromatic, small, white, nonelevated spots	Violaceous, flat-topped, angular, elevated papule
Late lesion	Large or small, parchment-like, atrophic depigmented areas	Large or small, parchment-like atrophic, depigmented areas	Large or small, atrophic areas; most of these are hyperpigmented, but occasionally without pigment
Plugging of follicles	Almost invariably present	May be present	May be present
Confluence of lesions	Is the rule	Is the rule	In some cases
Extent of lesions	Variable	Variable, but usually only a few	Usually fairly generalized, though atrophic lesions may be present in only a few areas
Lesions of the mouth	Occasionally present	Very rarely, if ever, present	Commonly present
Essential pathology	Sclerosis of connective tissue with disappearance of the elastic tissue which begins in the papillary layer; this has hyperkeratosis of the stratum corneum, atrophy of the prickle cell layer with disappearance of the rete pegs and papillae as a result; there is perivascular infiltrate of round cells beneath the sclerotic band; with progress of the disease this band becomes wider; follicular plugging is usually present	Early there is disklike sclerosis of the connective tissue and a disappearance of the elastic tissue of the upper cutis; at the border of the sclerosis there are small collections of round cells both perivascular and independent of the vessels; atrophy of the epidermis results from the sclerosis of the underlying connective tissue; plugging of the follicular orifices is not frequent; as the disease progresses, the sclerosis band becomes wider and the epidermal atrophy more marked	Even in the late atrophic stages moderate residues of the sharply limited, diffuse infiltrate of small round cells are found in the papillary and subpapillary regions of the cutis; there is atrophy of the prickle cell layer and absence of the rete pegs and papillae; there is some destruction and sclerosis of the connective tissue of the upper cutis by the cell infiltrate; the elastic tissue is almost completely destroyed also, only a few remnants remaining

SUMMARY

Because the three cases presented are each so typical of the disease represented, a résumé can be best made by comparison and contrast of the generally accepted clinical and pathologic aspects of the three diseases. Such a classification is given in the accompanying table.

From a consideration of the table and the three cases presented, it will be seen that an analysis of the symptoms, elementary lesions, observations on the skin and pathologic picture of a doubtful case will enable one to make an accurate diagnosis. If all factors are evaluated

there should be no difficulty in differentiating lichen sclerosus et atrophicus (Hallopeau) from either cardlike scleroderma or lichen planus with atrophy.

CONCLUSIONS

From this study I think that the following conclusions may be safely drawn:

1. Lichen sclerosus et atrophicus (Hallopeau) should be put in a category distinct from lichen planus with atrophy and cardlike scleroderma.

2. With it should be placed, at least provisionally, lichen albus (Zumbusch) and chronic atrophic lichenoid dermatitis (Csillag).

3. Cardlike scleroderma (Unna) and white-spot disease should be considered identical varieties of circumscribed scleroderma.

4. Lichen sclerosus et atrophicus (Hallopeau) and cardlike scleroderma (Unna) are similar histologically and must be differentiated on clinical observations.

5. Lichen planus in the atrophic stage still shows easily recognizable clinical and pathologic characteristics of the disease.

6. When lichen planus with atrophy occurs in the scalp it gives rise to a permanent atrophic alopecia.

LYMPHOBLASTOMA

A REPORT OF TWO CASES *

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We have recently had the opportunity to study two cases of cutaneous tumor formation. We found that these tumors consisted of small round cells which we considered to be of lymphoblastic derivation. These two cases were presented at the New York Academy of Medicine and there was a divergence of opinion as to whether the condition was leukemia, Hodgkin's disease, lymphosarcoma or mycosis fungoides. One of them was regarded clinically as a case of either Hodgkin's disease or lymphosarcoma; the other, as either mycosis fungoides d'emblee, leukemia or cutaneous sarcoma. Biopsies from these cases were presented to several authorities. In our first case, opinion as to diagnosis varied from Hodgkin's disease to leukemia to lymphosarcoma. In the second case, the opinion was that the condition was lymphosarcoma or a small cell sarcoma. In an attempt to classify our cases definitely we studied pertinent literature and found that there were two trends of thought on the part of those who had attempted to deal with this subject. The one classifies leukemia, pseudoleukemia, lymphosarcoma, Hodgkin's disease and mycosis fungoides under the general heading of lymphoblastoma. The other attempts to differentiate sharply each of these conditions as definite disease entities.

REPORT OF CASES

CASE 1.—*History.*—L. E. W., a white man, aged 62, American born, an engraver, had had the usual diseases of childhood; otherwise his personal history was unimportant. His mother had died at the age of 86 of general debility and his father had died at the age of 75 of an unknown cause. Six borthers and one sister were all living and well. There was no history of tuberculosis, cancer, nephritis, syphilis or insanity.

Present Illness.—The present illness began in the spring of 1925. The patient noticed painless swellings of the glands in the anterior cervical areas. He consulted a physician who made a diagnosis of probable Hodgkin's disease. The usual laboratory tests and physical examination were essentially negative at this time except for the glandular enlargement. He was treated with quinine, arsenic

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and iron for one year without any noticeable result. The patient left for France in April, 1926, and shortly after this time he found that the cervical glands had increased in size. He went to the American hospital in June, 1926, and from there was referred to Dr. Summer Jackson, who, after a careful examination, repeated blood counts and Wassermann test, made a diagnosis of probable Hodgkin's disease. The patient refused a biopsy at this time. He was then referred to Dr. Cheron, who applied roentgen therapy to the cervical glands. He received three exposures at weekly intervals, the swelling of the glands completely disappearing after the last exposure. He then returned to America and remained comparatively free from symptoms until September, 1927, at which time he noticed a peculiar irritative sensation on the tongue. Examination by Dr. Imperatori, on Oct. 17, 1927, showed considerable enlargement of the lingual tonsil with slight enlargement of the lower edge of the epiglottis. Examination also showed a mass 0.5 by 0.25 cm. on the right side beginning just beyond the arytenoid and extending laterally into the aryepiglottic fold. The Wassermann reaction was negative. He was then referred for roentgen treatments and received several of these. He was seen again by Dr. Imperatori in May, 1928, who found a mass 3 by 4 cm. located in the right aryepiglottic fold which interferred considerably with the patient's breathing. There were also glandular enlargements in the axillae and popliteal fossae. On May 21, 1928, a tumor mass, which was included in the right aryepiglottic fold, was removed surgically by Dr. Imperatori. A much smaller mass of tissue was also removed from the region of the left aryepiglottic fold at this time. The histologic report was that of lymphocytoma showing a low grade malignancy. In August, 1928, the right eye began to bother him. He consulted Dr. Shine who found five small tumors, varying in size from that of a split pea to that of a hazelnut, in the upper lid of the right eye. These were underneath the skin, were freely movable and were rather firm. He also found two smaller tumors in the left upper and lower eyelids near the inner canthus. On the trunk, left side of the neck and on the arms there were several isolated small tumors. On Sept. 12, 1928, the tumors from the right upper eyelid were removed surgically. The histologic report was that of lymphoma. On Oct. 12, 1928, the patient was referred to one of us by Dr. Shine who found single and bunched, painless, nodular, subcutaneous masses from 0.25 to 2 cm. in diameter scattered over the trunk, eyelids and upper extremities and also a bilateral cervical adenopathy which was more marked on the left side. In November, 1928, one of these masses was removed from the left upper quadrant of the abdominal wall. The histologic report was that of a lymphosarcoma. At this time the patient was presented at the Dermatological Section of the New York Academy of Medicine, and the opinions varied between Hodgkin's disease and lymphosarcomatosis. The glands and tumors responded readily to roentgen therapy. The swellings disappeared entirely.

Physical Examination.—The patient was of medium height, weighed 182½ pounds (82.8 Kg.) and was fairly well nourished. There were numerous nodular lesions about 1 cm. in diameter scattered throughout the skin. There was a pea-sized, nodular growth at the inner angle of the left eye. The nose and mouth were normal. The cervical glands of both sides were enlarged and indurated, more so on the left side, where they fused into a mass the size of a small fist. The lungs were essentially normal. The heart was apparently enlarged to the left; sounds were regular and of good quality; there were no murmurs or thrills. The abdomen was soft. The spleen could be felt 6 cm. below the sixth costal cartilage at the end of inspiration. The liver was felt just below the costal border.

There were several glandular enlargements in the skin, some of which were close to each other and mainly felt over the splenic area. There was a tumor mass

the size of a hazelnut in the left epididymis. The blood pressure was 148 systolic and 98 diastolic.

Examination of the Blood.—April 2, 1929: The red corpuscles numbered 4,890,000 per cubic millimeter and were uniform in size. The leukocytes numbered 10,000 per cubic millimeter. The differential count showed: small lymphocytes, 31 per cent; large mononuclear cells, 6.5 per cent; polymorphonuclear neutrophils, 60 per cent; eosnophils, 2.5 per cent; mast cells, none. The hemoglobin was 83 per cent (14 Gm. per hundred cubic centimeters). The color index was 0.88. *Plasmodia malariae* were not found. On April 20, 1929, the red corpuscles num-

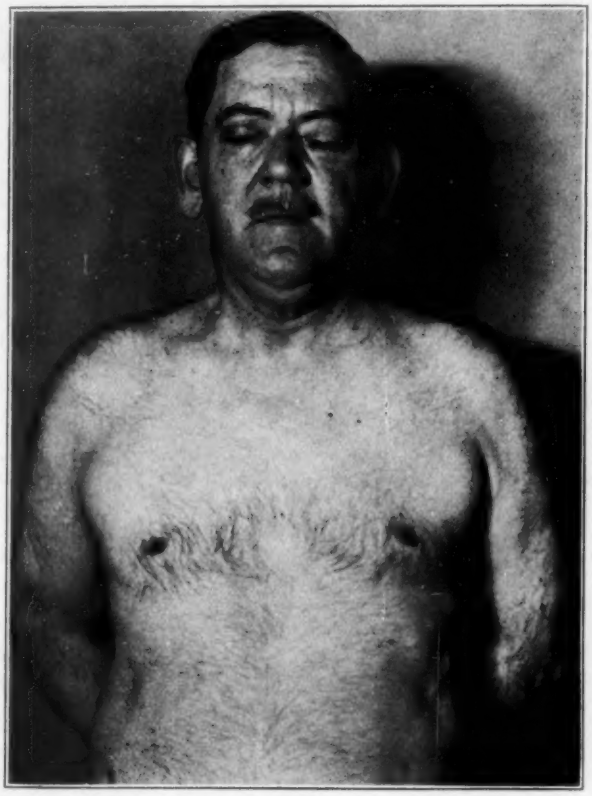

Fig. 1 (case 1).—Cervical, submaxillary and anterior axillary adenopathy with subcutaneous nodules on the left side of the trunk.

bered 4,880,000 per cubic millimeter and were uniform in size. The leukocytes numbered 7,600 per cubic millimeter. The differential count showed: small lymphocytes, 24 per cent; large mononuclear cells, 8.5 per cent; polymorphonuclear neutrophils, 66 per cent; eosinophils, 1 per cent; mast cells, 0.5 per cent. The hemoglobin was 83 per cent (14 Gm. per hundred cubic centimeters). The color index was 0.88. No *Plasmodia malariae* were found. On June 4, 1929, the erythrocytes totaled 4,100,000 per cubic millimeter and were uniform in size and shape; the leukocytes numbered 6,650 per cubic millimeter. The differential leukocyte count showed: polymorphonuclear neutrophils, 34.5 per cent; small lymphocytes,

57.5 per cent; large mononuclear cells, 8 per cent; eosinophils, none; immature polymorphonuclears, 2 per cent. The hemoglobin was 70.5 per cent (11.9 Gm. per hundred cubic centimeters). The color index was 0.85 per cent. *Plasmodia malariae* were not found. The specimen showed a moderate diminution in the amount of hemoglobin and in the number of red cells with a normal total leukocyte count, but a moderate lymphocytosis.

The Wassermann reaction on April 20, 1929, with beef heart cholesterinized and Kolmer antigens was negative; the Kahn precipitation test was negative.

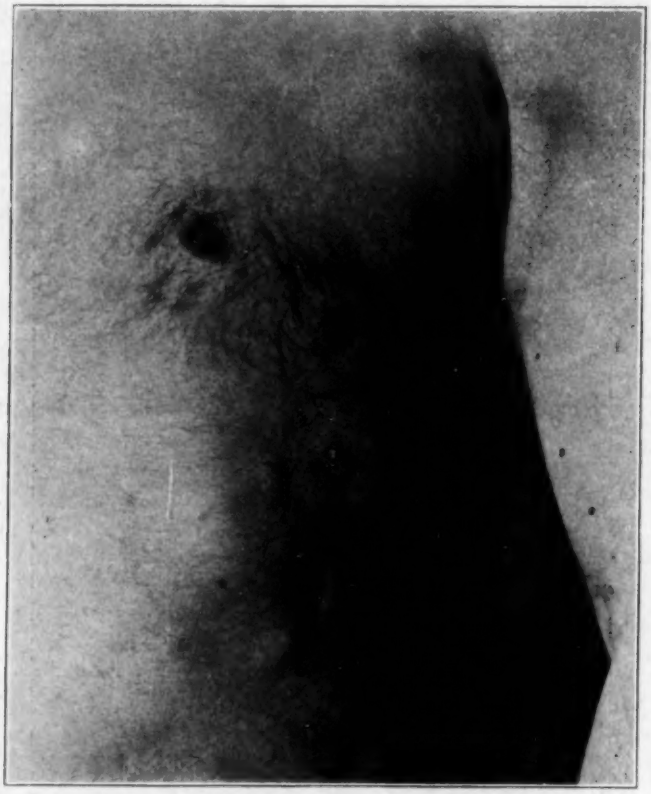

Fig. 2 (case 1).—Clearer view of subcutaneous nodules.

Chemical Examination of the Blood.—April 3, 1929: The urea nitrogen was 13 mg. and the uric acid was 5 mg. per hundred cubic centimeters of blood. The blood sugar was 0.104 per cent; the carbon dioxide-combining power of plasma per hundred cubic centimeters was 66.4 per cent. The hemoglobin was 15.6 Gm. per hundred cubic centimeters. On April 3, 1929, the icterus index was 7.8. The van den Bergh test, direct, was negative, and the indirect was also negative; the Fouchet test was negative.

Urinalysis.—April 3, 1929: The specific gravity was 1.034; the color was amber and the reaction was acid. Tests for albumin, sugar, acetone and diacetic acid were negative. Indican was one plus. No casts, pus or blood was found. There was a large amount of amorphous débris and an occasional leukocyte.

Examination of Feces.—April 2, 1929: The feces were brown and offensive. Grossly there was no admixture. The approximate amount of bile pigment was normal; there was no unconverted bile pigment. The consistency was pasty; the reaction was acid. Albumin putrefaction was absent; carbohydrate fermentation was slight, and the amount of unconverted starch was slight. Blood pigment "occult" was positive. Microscopic examination showed only a few striped muscle fibers, a small amount of vegetable remnants and a moderate amount of granular detritus. There were no parasites, ova or blood cells. A few pus cells and a small amount of mucus were observed. Free fat was not present. The fatty acids were not excessive. The flora was chiefly gram-negative.

Roentgen Examination.—April 6, 1929: The roentgenographic examination of the right hypochondrium showed no evidence of concretions in the gallbladder.

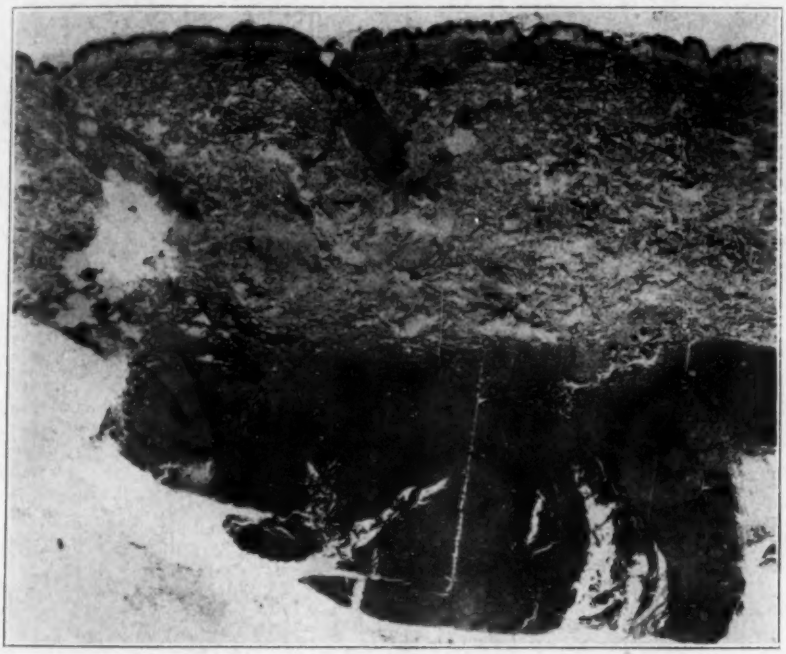

Fig. 3 (case 1).—Situation of the tumor and the extension along the follicle toward the surface indicating an invasive nature; low power magnification.

The fluoroscopic examination of the stomach showed no irregularities. The fluoroscopic and roentgenographic examination of the chest and posterior mediastinum showed a multiple general enlargement of the aorta and also of the left side of the heart. The lungs appeared to be clear and well aerated. The posterior mediastinum appeared to be clear. The roentgenographic examination of the right thigh and lower leg showed no bony changes in the femur, fibula or tibia. The roentgenographic examination of the sella turcica showed the clinoid processes to be irregular as if destructive changes were present. The entrance to the sella was narrow, but the sella appeared normal in depth. The fluoroscopic and roentgenographic examination of the large intestine showed a marked redundancy of the pelvic colon but no other irregularities in the large bowel. The appendix appeared to be long, well filled and not tender.

Special Examination of Cutaneous Lesions: There was a bilateral cervical adenopathy, much more pronounced on the left side where the glands seemed to have coalesced slightly in the supraclavicular fossa. The glands on the left side were 5.2 cm. in diameter; those on the right were 2 cm. in diameter. The glands in these areas were firm and rather hard but painless. Their borders and outlines could be easily made out. Both submaxillary glands were moderately enlarged. In the right axillary region there were a few firm glands from 1 to 2 cm. in diameter. The epitrochlear glands were readily palpable. There was no inguinal adenopathy. On the upper and lower left eyelids, there were two subcutaneous nodules 0.5 cm. in diameter. On the right upper eyelid there were three subcutaneous nodules measuring 0.5 cm. in diameter. In the left preauricular

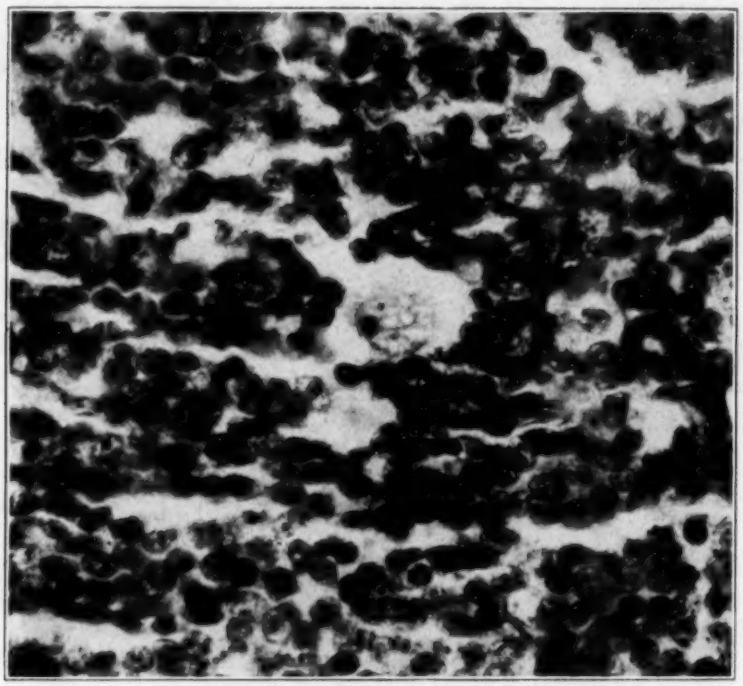

Fig. 4 (case 1).—Tumor cells showing their lymphoid nature. Many mitotic figures and endothelial leukocytes were noted; high power magnification.

region there was a nodule 1 cm. in diameter. Scattered over the front and back of the arms, forearms and trunk were numerous nodules. These nodules varied from 0.5 to 2.5 cm. in diameter. They were apparently subcutaneous. The skin over them was easily moved, and they were in no way adherent to the underlying tissue. They were apparently just beneath the derma and were easily outlined. Some were globular and some were oval; their borders could be easily felt. They were firm but not tender.

Histologic Report.—The sections examined from this case were those of a nodule with the overlying skin. The nodule measured 1 by 0.5 by 0.5 cm. The section showed an epidermis which except for a flattening of the papillae over the topmost portion of the underlying tumor was practically normal. The superficial

cutis consisted of a loose network of connective tissue. In this area there were spindle-shaped cells and cells of lymphocytic type in numbers more numerous than those seen in the normal cutis. The outstanding pathologic changes were situated deep in the cutis. These consisted of a nodule which extended partly into the hypoderm. This nodule was circumscribed but possessed no definite capsule. A number of processes extended from the nodule and penetrated between the collagen bundles. Several tiny satellite nodules were present. These infiltrations were well marked in the region of the coil glands. There were others in the vicinity of the pilosebaceous organs along which they extended almost to the surface epithelium. Collagen bundles were absent from the tumor, and only a fine connective tissue reticulum remained. The blood vessels of the tumor masses were few in number and were fairly thick walled. They did not possess the characteristics of newly formed vascular channels. The blood within the vessels showed no abnormal number of leukocytes. Red blood corpuscles were found free in the connective tissue. These hemorrhages were undoubtedly recent and were principally the result of the trauma of excision and injection of procaine hydrochloride. The tumor and its satellite nodules, as well as its processes, consisted of closely packed, small round cells which suggested lymphocytes more than any other tissue cells. These cells were much alike in their characteristics. They were a little larger than a lymphocyte; they were round; their cytoplasm was scanty. The nuclei in the preponderant mass of cells were also round. They contained much chromatin material, but they each showed a distinct nucleolus. Many mitotic figures were seen which suggested that the tumor was growing in situ and was not entirely due to a deposit of cells from an outstanding focus. Among this mass of similar cells were a few large cells of two varieties, i. e., mass cells with their metachromatic granules which were demonstrated by cresyl violet staining and large uninucleated and occasionally multinucleated cells with vesicular nuclei and prominent central nucleoli. The latter cells contained a considerable amount of evenly staining cytoplasm. Many of these cells also contained inclusion bodies of a deep basophilic character. This picture suggested that the cells were endothelial leukocytes which contained the nuclear remains of tumor cells. Silver preparation of this tissue showed a fine silver positive reticulum which divided the tumor into lobules. Fine processes of this reticulum extended in many instances between the individual cells.

CASE 2.—*History.*—M. J. R., a white man, aged 38, American born, an automobile mechanic, noticed the appearance of two skin-colored, painless, cutaneous growths, the size of a pigeon's egg, on the outer left thigh and on the back of the right thigh two months before presentation. Previous to this the patient was apparently in good health. This patient was a private case of Dr. Dillingham who permitted us to study him.

The lesions gradually increased in size and acquired a reddish color. At the same time several other lesions appeared on the front of the thighs, legs and right forearm. One week after the onset, the penis began to swell and became markedly edematous with weeping of the glans. One month later the patient began to breathe with difficulty and became hoarse. This condition has become progressively worse. Six weeks from the time of onset the patient noticed swelling of the testicles. This swelling has become marked.

Present Illness.—The patient had several tumor growths, varying from 2 to 5 cm. in diameter, scattered over the thighs, buttocks, legs and forearms. These lesions were skin colored, definitely cutaneous, painless and soft. They resembled a red tomato attached to the skin. Some seemed to be attached to the skin by a fairly broad pedicle. The testicles were stony hard but were not painful unless

marked pressure was exerted. The penis was markedly swollen and red and was unquestionably part of the same process. The inguinal glands were enlarged. There was a slight general glandular adenopathy. The patient was hoarse and had some difficulty in breathing. The tumors responded rapidly to unfiltered radiation. The biopsy report was that of lymphosarcoma.

Physical Examination (Courtesy of Memorial Hospital).—The uvula was pushed well down and backward; it felt firm but not hard. There was a fairly large growth at the base of the tongue extending down into the left pyriform sinus; it had a white, finely fungated surface about 2 cm. in diameter. The

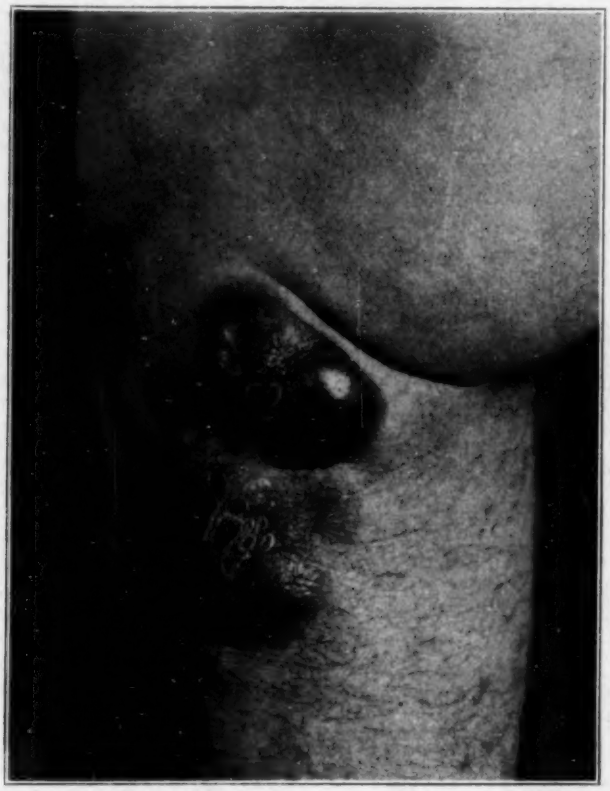

Fig. 5 (case 2).—Large, red, cutaneous and subcutaneous tumors.

epiglottis and arytenoids were not involved. There was no cervical adenopathy. The lungs were essentially normal. The heart was not enlarged; the rhythm was irregular, an occasional definite extrasystole and frequent coupling being present; sounds were all of good quality and there were no murmurs. The abdomen was normal. There was pitting edema of the right leg from the midtibial region to the foot, and the skin was reddened and glazed.

Laboratory Reports.—The Wassermann reaction of the blood was negative. The blood count, on May 18, 1929, showed: erythrocytes, 3,610,000 per cubic millimeter; the red blood cells were uniform in size and shape; the leukocytes numbered 10,100 per cubic millimeter. The differential leukocyte count was:

polymorphonuclear neutrophils, 45.5 per cent; small lymphocytes, 41.5 per cent; large mononuclears, 12.5 per cent; eosinophils, 0.5 per cent; basophils, none; immature polymorphonuclears, 13 per cent. The hemoglobin was 79 per cent (13.4 Gm. per hundred cubic centimeters). *Plasmodia malariae* were not found. The color index was 1. The specimen showed a slight diminution in the amount of hemoglobin and in the number of red cells. There was a slight leukocytosis with a normal percentage of polymorphonuclears, but a slight rise in the percentage of immature polymorphonuclears.

Biopsy Report.—On May 29, 1929, the biopsy report was: malignant tumor, lymphosarcoma or lympho-epithelioma, probably the latter.

Roentgenologic examination of the chest, on May 29, 1929, showed no evidence of enlarged mediastinal glands.

Special Examination of Cutaneous Lesions.—There was no cervical adenopathy. The axillary glands were definitely enlarged and their outlines could easily be made out. They were firm but not painful. The inguinal glands were also

Fig. 6 (case 2).—Two tumors on glans penis.

enlarged and firm. There was a diffuse swelling in the right popliteal region but no discrete nodes could be felt. Scattered over the forearms, buttocks, thighs and legs were numerous cherry-colored cutaneous and subcutaneous nodular lesions from 2 to 5 cm. in diameter. These lesions occurred singly. Some were definitely subcutaneous while others were cutaneous and elevated. The small lesions were skin colored, slightly elevated and presented a smooth surface. They were rather firm and painless and were moderately adherent to the skin. The larger lesions, most of which were on the outer surface of both thighs, were rounded, smooth, purplish-red, elastic, tumor masses which seemed to be attached to the skin by a broad pedicle; they were movable with the skin. Most of these growths showed areas of telangiectasia. Scattered here and there were infiltrated pinkish-red plaques. The penis was edematous. The right testicle was enlarged about 8 cm. in diameter; portions of it were firm but most of the upper pole felt cystic but was not tender. On the glans penis there were nodules which were red and firm and which were infiltrated and showed superficial ulceration.

Histologic Report.—Sections of skin were removed from the thigh. The section which was removed before roentgen therapy showed a loose keratin layer.

The granular layer was thin and consisted of one or two lines of cells in which some of the nuclei were swollen. The malpighian layer varied in thickness. In places it appeared to be atrophic, in others hypertrophic. A moderate intracellular and intercellular edema was noticed. There was no definite pigment in the basal cell layer. The corium was infiltrated throughout by cells which formed nests and strands, and there was a rather large conglomeration in the hypoderm. Many of the papillae were obliterated. In many places a narrow band of connective tissue just beneath the epidermis was found to be free from cellular infiltration. The main tumor mass was deep in the skin and the adjacent subcutaneous fat. This tumor mass was composed of cells which were fairly uniform in their

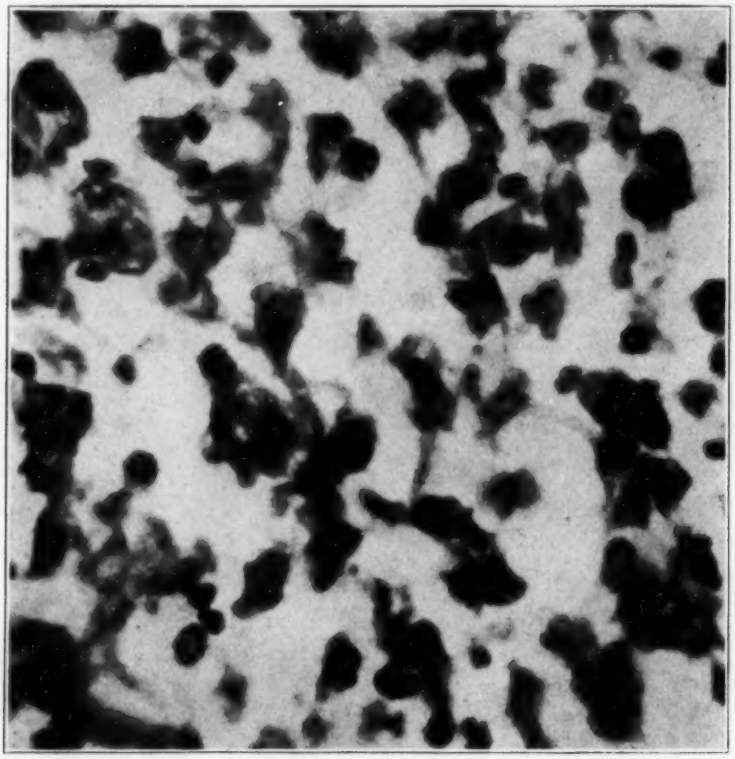

Fig. 7 (case 2).—Some shrinkage of cells resembling immature lymphoid cells; high power magnification.

appearance and which extended along the coil glands and hair follicles and formed large nests in the corium. Tumor cells also infiltrated between the individual collagen fibers. The tumor cells were fairly large, larger than a lymphocyte. There were many, however, which were about the size of a lymphocyte and had its general characteristics. The nuclei were oval and chromatic. The cytoplasm was scanty. Most of the cells were twice the size of the smaller ones. The nuclei of these larger cells were round, oval, also irregular and somewhat lobulated. The lobulated forms were not numerous. The nuclei stained deeply. The nucleoli could be distinguished. The cytoplasm which conformed more or less with the shape of the nuclei in its outline was relatively more profuse than

that of the small cells. A great many of these larger cells showed mitotic figures in various stages of development. In the tumor masses there was a definite connective tissue network the cells of which seemed to be proliferating. The blood vessels were fairly numerous in the tumor masses. The coil glands were pushed apart by the infiltrating cells, but a definite connective tissue membrane could be distinguished about the glands.

Sections of the skin removed after roentgen threapy showed a somewhat similar appearance. The infiltration was not so dense as that of the skin before roentgen treatment was begun. The general appearance was more that of granulomatous tissue. The larger cells were fewer in number. The cells resembling lymphocytes

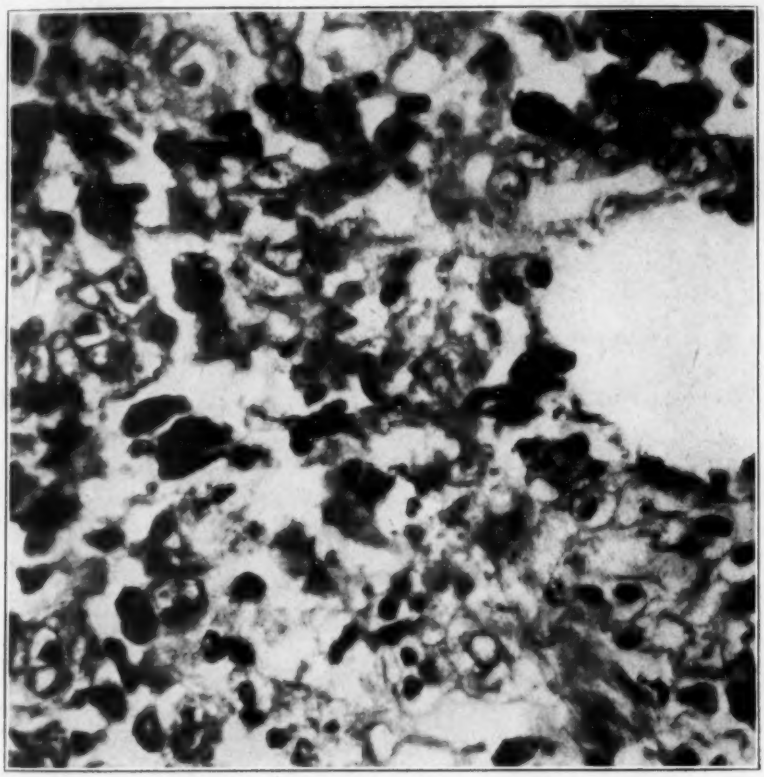

Fig. 8 (case 2).—Polymorphism of cellular infiltrate, lymphoid cells and cells of epithelioid characteristics after roentgen therapy; high power magnification.

were relatively more numerous. There was more evidence of edema in the superficial portions of the corium. The infiltrate seemed to come much closer to the epithelial layer. The collagen bundles did not appear to be so large, and many of them seemed to be fragmented. Silver impregnation of this section disclosed a definite silver positive reticulum which enclosed the individual cells. The elastic tissue was almost wholly destroyed in the region of the infiltrating tumor. This was demonstrated by an orcein stained slide. Only a small amount of connective tissue appeared in the tumor nodules. The larger collagen bundles showed a definite change in their staining characteristics and took both the red and the green of Masson's trichrome stain. This was presumably due to the changes which

had occurred after roentgen therapy. In the trichrome stained sections the infiltrate appeared to be polymorphous. There were many large cells with vesicular nuclei and prominent nucleoli. Between these cells were scattered many small round cells which showed much scantier cytoplasm the nuclei of which were pyknotic. These cells resembled lymphocytes closely. Although the infiltrating cells formed nodules, they were also scattered throughout the section. Mitotic figures were seen but not to the degree described in the previous sections removed in this case. Many more, however, were visible than in the sections removed from the first case.

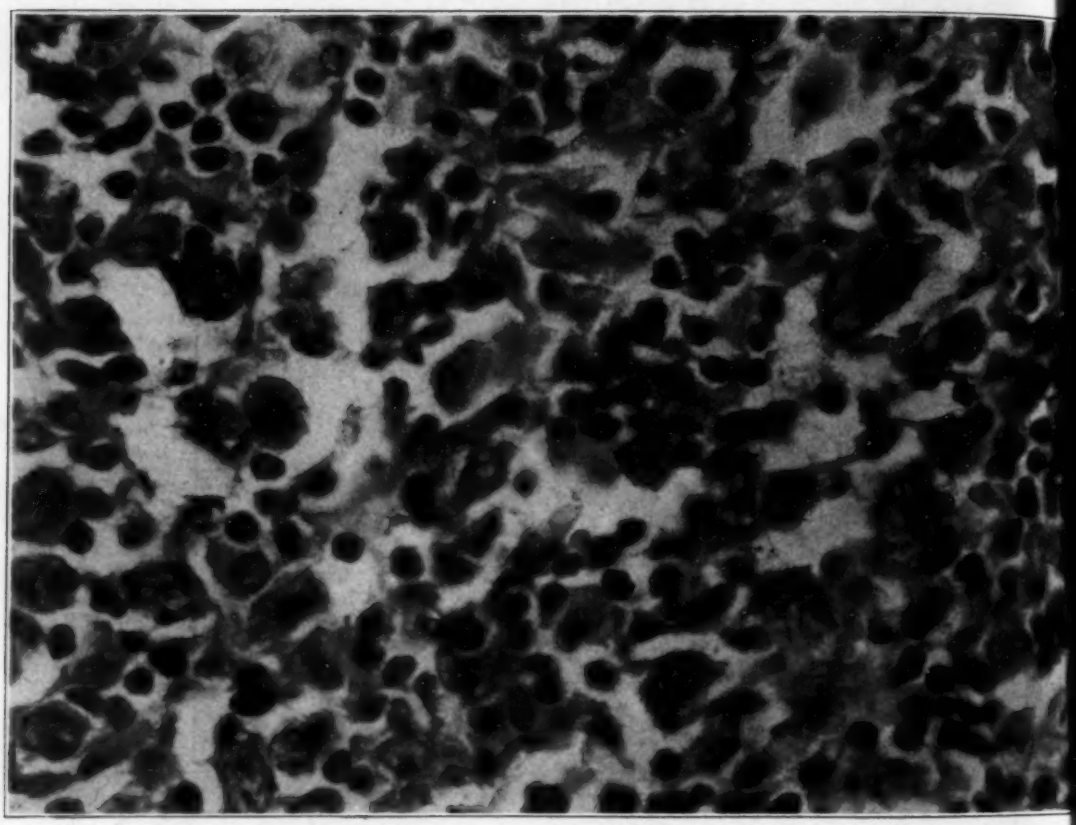

Fig. 9.—Polymorphism of the cellular infiltrate which consists of lymphoid as well as many epithelioid cells and large Reed cells in Hodgkin's disease; high power magnification.

COMMENT

In examining the two cases which we are reporting, we thought that the condition resembled lymphosarcoma more closely than any other disease. In view of the difference of opinion, however, of other men to whom the problem of classifying these two cases was submitted, we referred to the general literature on this subject and found that the same divergence of opinion was here presented. Because of this, we

submit what we, ourselves, and others considered typical cases of mycosis fungoides, Hodgkin's disease and lymphatic leukemia which we shall compare with these cases of presumable lymphosarcoma and attempt to show that they are so overlapping in their characteristics that it is well nigh impossible sharply to differentiate them one from the other.

The section of mycosis fungoides shows an epidermis which is covered by a few loose scales of keratin material. Parakeratosis is present. There is practically no granular layer to be seen. The prickle

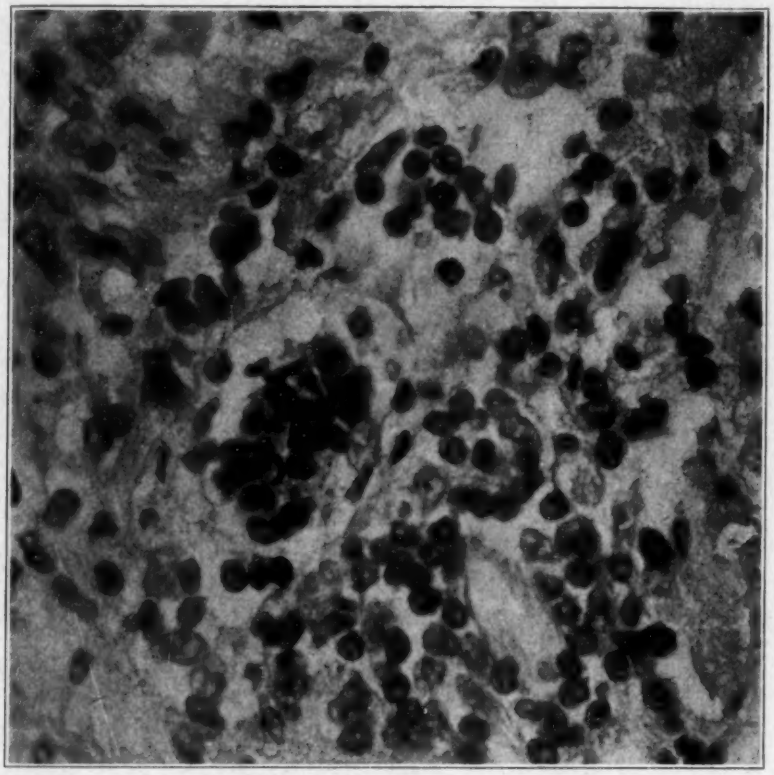

Fig. 10.—Lymphoid cells and cells of epithelioid and endothelioid nature in lymphatic leukemia; high power magnification. Note the cells in the capillary.

cells show edema, and this layer shows a definite hypertrophy. The rete pegs are prolonged. The papillae are infiltrated with round cells of lymphoblastic type. There is an increased number of fibroblastic cells. This infiltration is also profuse. There are many cells with elongated bodies and pyknotic nuclei. The cytoplasm is scanty. A few cells with large vesicular nuclei with a large amount of cytoplasm which is homogeneously stained are present. The majority of cells appear to be of a lymphocytic type. Scattered among these are fusiform cells

and occasionally eosinophils. The cresyl-violet stain discloses only an occasional mast cell. By silver impregnation a profuse silver positive reticulum separates the individual cells into tiny nests separated one from another.

We also present a section from a typical Hodgkin's node. This shows many epithelioid cells. Some are elongated and some are triangular or polygonal. Scattered among these are numerous multi-

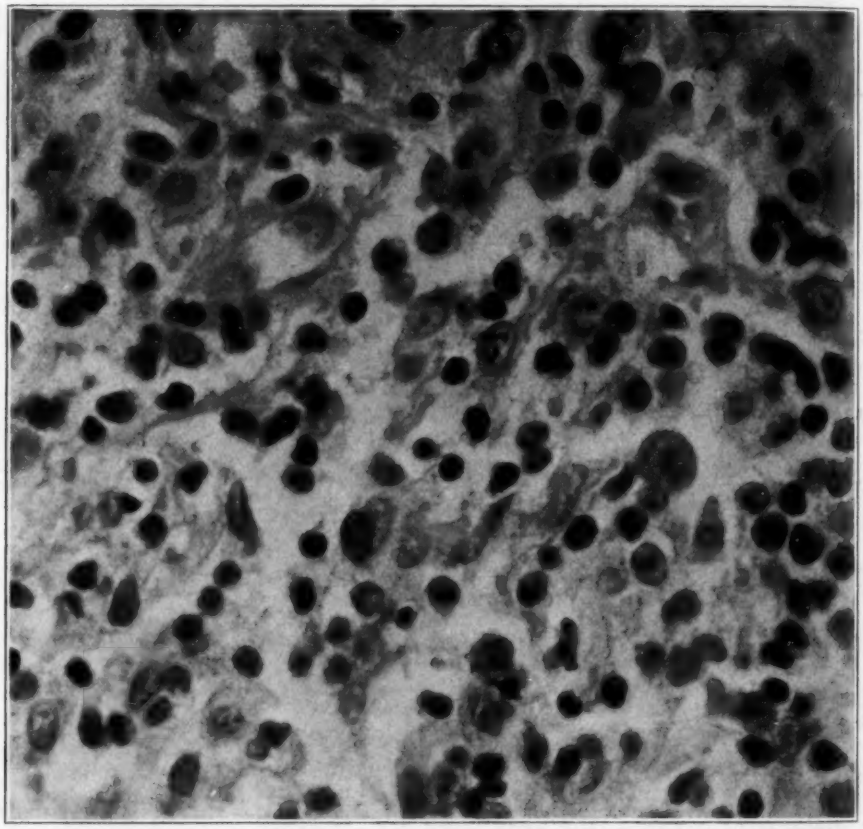

Fig. 11.—Polymorphic infiltration consisting of lymphoid cells and cells appearing to be epithelioid and endothelioid in nature in mycosis fungoides; high power magnification (courtesy of Dr. L. W. Ketron).

nucleated cells. Some of them appear to have lobulated nuclei. They are considerably larger than the former. The epithelioid cells have elongated and oval vesicular nuclei which are barely visible. The multinucleated cells are the more chromatic, but their nuclei are also vesicular. Their cytoplasm is homogeneous. Among these cells are seen many small round forms of a lymphocytic character. In places they are seen as isolated units; in others, they form rather definite

masses. In this particular section no eosinophils are noted. A few endothelial leukocytes are seen to contain chromatic granules. An occasional cell shows mitotic figures. No plasma cells are seen. Here and there trabeculae of connective tissue are noted running through the tumor mass.

A section from a typical case of lymphatic leukemia shows a crust consisting of fibrin, polymorphonuclear leukocytes and colonies of bacteria. Much cellular débris and products of nuclear degeneration are also present in this crust. Beneath this crust the skin shows a definite necrosis which extends into the corium. Subepidermal vesicle formation has taken place. A definite granulation tissue is formed at the bases of these vesicles. This granulation tissue shows many polymorphonuclear lymphocytes and young fibroblasts. There is a marked edema throughout the corium. The keratin layer is thin but definite. The rete pegs are somewhat elongated in places; in others, they are obliterated. The major portion of the corium shows diffuse infiltration of round cells. This extends into the lobules of fat tissue. These round cells are of lymphocytic type with typical deeply staining nuclei and scanty cytoplasm. Definite collections of these cells are seen. It is among these masses of wandering cells that epithelioid and endothelioid cells are noted. The latter forms possess vesicular nuclei and a greater amount of cytoplasm. They are elongated and larger than the cells of lymphoblastic origin. The coil glands are separated by masses of the small round cells. The infiltrate of lymphoblastic cells seems to follow the coil gland ducts toward the surface coming into close proximity with the epithelium. No eosinophils are seen. Many of the blood vessels contain large numbers of round cells which resemble lymphocytes.

Mallory [1] grouped the conditions that we have discussed under the name of lymphoblastoma. Keim [2] recently described a series of cases that fall in this group and proposed the continuous usage of lymphoblastoma at least until more is known of its etiology. Hazen and Strobel,[3] Cole,[4] Fraser,[5] Highman [6] and others have pointed out close

1. Mallory, Frank B.: Principles of Pathologic Histology, Philadelphia, W. B. Saunders Company, 1914.

2. Keim, Harther L.: Lymphoblastoma: Their Interrelationships, Arch. Dermat. & Syph. **19**:533 (April) 1929.

3. Hazen, H. M., and Strobel, E. R.: Mycosis Fungoides in the Negro, J. Cutan. Dis. **29**:147, 1911.

4. Cole, H. N.: The Cutaneous Manifestations of Hodgkin's Disease: Lymphogranulomatosis, J. A. M. A. **69**:341 (Aug. 4) 1917.

5. Fraser, J. F.: The Pathology of Mycosis Fungoides, J. Cutan. Dis. **35**:793, 1917.

6. Highman, Walter J.: Mycosis Fungoides and Kindred Conditions, Arch. Dermat. & Syph. **13**:522 (April) 1926.

similarity in this group and have emphasized the fact that they should be classified collectively rather than separately. From the time of Virchow to the present day, there is a difference of opinion in regard to this question. Virchow could not understand why lymphosarcoma, a condition which resembled lymphatic leukemia so closely, left the blood unchanged. We now know that any one of these conditions after persisting for some time may cause a blood picture of leukemia to develop. Kundrat,[7] Paltauf and others attempted to separate lymphosarcoma from leukemia. Ziegler,[8] Fraenkel,[9] Webster [10] and Longcope [11] believed that Hodgkin's disease is a separate entity. Pardee and Zeit [12] stated that there has been an attempt on the part of various observers to place mycosis fungoides first in the category of sarcoma, then to consider it as a type of infectious granuloma although no infectious change or source of infection has been described; third, as a form of lympho-adenoma; fourth, as a cutaneous expression of a leukemic process, and finally, as an independent pathologic entity.

Cutaneous lymphatic leukemia may be divided into two types, the circumscribed and the universal. According to Arndt,[13] the circumscribed form consists mainly of small lymphocytes, whereas the universal form consists of large lymphocytes which are more closely related to the lymphoblasts and have numerous mitoses. The sections usually show a zone free from infiltration in the papillary layer. Ketron and Gay,[14] in describing their case of universal lymphatic leukemia of the skin, could not corroborate Arndt's observations. They found that most of the cells in the cutis were small lymphocytes, although some of the larger forms may have been large lymphocytes or lymphoblasts. Furthermore, they found no mitoses, nor was the cell-free zone in the papillary layer present. Even the epidermis was invaded by lymphoid cells. It was their opinion that the cellular infiltration of the cutis in this disease is not necessarily confined to a definite lymphatic cell type but may vary depending on the age of the cells liberated from the blood stream and perhaps on their further development in the tissues.

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7. Kundrat: Wien. klin. Wchnschr. **6**:211, 1893.

8. Ziegler: Die Hodgkinsche Krankheit, Jena, Gustav Fischer, 1911.

9. Fraenkel: Verhandl. d. deutsch path. Gesellsch., April, 1912, p. 5, fifteenth session.

10. Webster, L. T.: Lymphosarcoma, Lymphatic Leukemia, Leukosarcoma, Hodgkin's Disease, Bull. Johns Hopkins Hosp. **31**:458 (Dec.) 1920.

11. Longcope, W. T.: On the Pathological Histology of Hodgkin's Disease with a Report of a Series of Cases, Bull. Ayer Clin. Lab. Penn. Hosp. **1**:4, 1903.

12. Pardee, L. C., and Zeit, F. R.: Mycosis Fungoides, J. Cutan. Dis. **29**:7, 1911.

13. Arndt, quoted by Ketron and Gay (footnote 14).

14. Ketron, L. W., and Gay, L. N.: Universal Lymphatic Leukemia of the Skin, Bull. Johns Hopkins Hosp. **34**:404, 1923.

From these opinions, as well as numerous others, it is practically impossible from a histologic point of view to draw a clear dividing line between any of the foregoing conditions. From our study of the two reported cases, as well as a study of the sections from the other diseases mentioned, we would not wish to go much further than to say that the cases fall into the lymphoblastoma group. We are speaking here solely about the histologic phase. We do not wish to be misunderstood, however. There are typical histologic and clinical pictures which are textbook in character and suggest fundamental differences between the individual subgroups of lymphoblastoma. These cases are not common, as every one who has interested himself in this problem has found. The only phenomenon which stands out is the unique blood picture of leukemia, but there is doubt today whether even this is necessarily pathognomonic, since a leukemic blood picture has been described in miliary tuberculosis and the so-called glandular fever or agranulocytic anemia. The Dorothy Reed or Sternberg cells considered to be characteristic of Hodgkin's disease would tend to separate this condition from the others; yet even this has been disputed.

These comments give some idea as to how difficult it may be to diagnose histologically the condition in cases such as we report. The clinical aspect of this problem is even more difficult to interpret without a typical blood picture. In view of the fact that the lymphoblastomas attack the blood-forming organs, principally the lymph nodes, there is always either a localized or a generalized adenopathy disregarding the lymphadenoses of Arndt or the leukemids of Audrey. One must still consider the cellular deposits in the cutaneous or subcutaneous tissues. Any one of these diseases may present adenopathy with cutaneous or subcutaneous nodules, as has been cited by Wende,[15] Fraser, Fox,[16] Cole and others. The cutaneous tumor formation may be either soft or hard, skin colored or dark red. The subcutaneous nodules, on the other hand, are usually firm. Some of these tumors, whether cutaneous or subcutaneous, may ulcerate. This may sometimes point in the direction of mycosis fungoides, but ulceration has been reported in the other conditions also. The liver, spleen and other organs may or may not be involved, and this does not help us regarding the clinical diagnosis. The blood picture may at first be subleukemic, then aleukemic and finally leukemic. A few observers have felt that Hodgkin's disease and mycosis fungoides had a definite blood

15. Wende, G. W.: A Case of Lymphatic Leukemia, Apparently Developing Out of Hodgkin's Disease, Accompanied by Leukaemic Lesions and Pigmentation of the Skin, Culminating in Streptococcus Infection, Am. J. M. Sc. **122**:836, 1901.

16. Fox, Howard: Lymphogranulomatosis of the Skin in Hodgkin's Disease, Arch. Dermat. & Syph. **2**:578 (Nov.) 1920.

picture, but too much stress cannot be laid on this fact. In all of these conditions there may or may not be preexisting or concomitant dermatoses.

In our first case we have a patient with an adenopathy of several years' standing. In addition to this, he has subcutaneous nodules with an enlarged liver and spleen. From a clinical point of view, his condition could be any one of the group of diseases we have described, with the exception of true leukemia. At the time of the writing of this paper, however, his blood picture is slightly suggestive of a leukemic termination. Histologically, up to this point we feel that the tumors are those of a lymphoblastoma of the type that many have called lymphosarcoma. The scanty silver positive reticulum suggests the atypical lymphosarcoma of the French pathologists. This is usually considered malignant. In this instance, its course has proved relatively benign.

In our second case, the picture is somewhat different, yet the histologic manifestations are consistent with the diagnosis of a lymphosarcomatosis variety. Here there is a slight adenopathy with several fairly large, protuberant, relatively soft, reddish tumors with a slight amount of infiltration extending into the subcutis. Clinically, the case suggests either a true sarcomatosis or a mycosis fungoides d'emblee. The two sections removed from this case differed from one another. The first, due to the uniformity of its cells, resembled a lymphosarcoma or an undifferentiated round cell sarcoma. The second section had the appearance of a granuloma of polymorphic characteristics and more nearly resembled mycosis fungoides or possibly Hodgkin's disease.

We have reported two cases which we think fall into the category of lymphoblastoma of the lymphosarcomatous type. Yet we feel that each has certain peculiarities common to both and certain other characteristics which force an admission of their similarity to leukemia, mycosis fungoides, undifferentiated round cell sarcoma and possibly Hodgkin's disease. After a study of the cases and the literature, we are uncertain where to place them; furthermore, we feel that we should group not only these presumable cases of lymphosarcoma but also cases of mycosis fungoides, leukemia, pseudoleukemia and Hodgkin's disease in a generic group of lymphoblastoma. When we are certain of the etiology, whether or not they are infectious processes or fall into the class of neoplastic diseases, we can classify them. The methods we are using at present, clinically and in the laboratory, are inadequate in aiding this purpose. While clinically the reported cases are different, histologically certain of the sections resemble one another in many respects. The first case histologically suggests either leukemia or lymphosarcoma; we feel that the latter diagnosis is, at the present writing, the more correct one for the reasons we have mentioned.

In reference to the second case, the section removed from one of the tumors was probably lymphosarcoma, whereas the other section simulated to some extent Hodgkin's disease or mycosis fungoides although lymphosarcoma was by no means an irrevelant diagnosis. It is possible that the difference between the first and the second sections was due to a small amount of irradiation which caused many of the lymphoid cells to disappear. Therefore, there are certain characteristics histologically common to the conditions that are grouped under the classification of lymphoblastoma. For this reason we have chosen the title of lymphoblastoma rather than lymphosarcoma.

SUMMARY

1. Hodgkin's disease, leukemia, mycosis fungoides and lymphosarcoma should probably be grouped under the general heading of lymphoblastoma.

2. Two cases have been reported which clinically are unlike but which histologically are related.

3. These two cases, which we have referred to as lymphosarcoma, are closely related clinically and histologically to the other types of lymphoblastoma.

4. While lymphoblastoma is only a tentative classification, it is impossible, in our opinion, to separate them clearly until the etiology is known.

5. We believe that clinically it is impossible to diagnose them definitely.

6. Even histologic examination leaves many vital questions unsolved.

DISCUSSION

DR. LLOYD W. KETRON, Baltimore: I have enjoyed the presentation by Drs. McCafferty and Machacek and believe that all works of this character tending to show a relation between diseases of this type are valuable. We should not lose sight, however, of the fact that pathologic reactions are most frequently types of reaction rather than specific reactions, and resemblances in microscopic appearance do not necessarily mean etiologic similarity.

DR. A. BENSON CANNON, New York: I am sure we all realize the great difficulty one experiences in making a clinical or even a pathologic diagnosis in such cases as described by the authors; especially is it hard to distinguish between Hodgkin's disease and lymphosarcoma. On three different occasions I have made a clinical diagnosis of Hodgkin's disease, the patient having the typical scratch papules, the thickened, brownish discoloration of the skin and even the loss of hair so frequently seen with that condition, and yet the final histologic diagnosis was that of lymphosarcoma. I recall one case in which a diagnosis of mycosis fungoides was made by several able dermatologists, later to be changed to one of Hodgkin's disease and finally, at autopsy two years later, there was a pathologic diagnosis of lymphosarcoma. Not many months ago I removed a small growth

from the nose of a patient; the condition had been diagnosed as a basal cell epithelioma but I suspected it to be a sarcoid and was surprised to receive from a number of our best pathologists the opinions that the man had either Hodgkin's disease or lymphosarcoma, no one being able to make a definite statement as to the nature of the growth. I believe any work such as Dr. McCafferty and Dr. Machacek have done to aid in establishing a basis for a definite diagnosis histologically for each of these diseases will prove of immense value to the internist as well as to the dermatologist.

Dr. Lawrence K. McCafferty, New York: There is a point brought out by Dr. Cannon which I should like to emphasize again. Whenever possible a gland should be removed in these cases for microscopic study, as many times the diagnosis may be made early in this group of diseases. A section from the skin will not always disclose the diagnosis, at least as quickly as a section from a gland.

POSTPUNCTURE HEADACHES

A CLINICAL AND EXPERIMENTAL STUDY OF THE CAUSE AND PREVENTION *

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In the section on dermatology and syphilology at the Mayo Clinic, approximately fifty spinal punctures are done weekly. The headaches that follow the procedure have been complained of by so many patients that it seemed wise to investigate the cause and search for some means of preventing them.

Based on explanations of the cause of the headaches, various procedures have been recommended for prevention or cure. With the idea of increasing either the pressure or the actual secretion of spinal fluid, subcutaneous injections of solutions of pituitary and the intravenous injection of hypotonic solution of sodium chloride have been used. The use of a needle of small caliber has been advised to reduce to a minimum the size of the hole left in the meninges. Sicard [1] and others have suggested confining the patient to bed with the head lowered for from twenty-four to forty-eight hours after puncture. Replacing the fluid removed at puncture with a physiologic solution of sodium chloride introduced into the canal with a syringe has been reported to be of benefit. Greene [2] suggested the employment of a needle with a rounded point and stated that by means of it, injury to the meninges similar to that produced by the usual bevel-pointed needle may be largely avoided. He has obviated postpuncture headaches in practically every case by the use of this needle.

In my experience none of these methods has been satisfactory; in fact, headaches continued to occur frequently following their use. In an effort to establish the cause of postpuncture headaches and to find some means for their prevention, several investigations were undertaken:

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* An abridgment of the thesis which was submitted in June, 1928, to the Faculty of the Graduate School of the University of Minnesota, in partial fulfilment of the requirements for the degree of Master of Science in Dermatology.

1. Sicard, J. A.: Le liquide céphalo-rachidien avec préface du Dr. Brissaud, Paris, Masson & Cie, 1902.

2. Greene, H. M.: Lumbar Puncture and the Prevention of Postpuncture Headache, J. A. M. A. **86**:391 (Feb. 6) 1926.

1. The relation to the incidence of headache of certain factors, such as the weight and temperament of patients and changes in spinal fluid pressure during lumbar puncture, was investigated.

2. The work of Jacobaeus and Frumerie [3] on the pressure of the spinal fluid before puncture and during the postpuncture period was repeated and a further observation was made in regard to the pressure during the headache.

3. To investigate the possibility of the occurrence of leakage of spinal fluid through the opening made by the needle in the dura mater at lumbar puncture, a portion of lumbar dura mater was examined post mortem from a patient on whom spinal puncture had been done eleven days before death.

4. In a series of experiments, pieces of catgut 4 cm. or more in length were inserted at lumbar puncture into the walls of the spinal canals of ten dogs and were left in place, filling the holes made by the needles. The purpose of this experiment was to test a method for

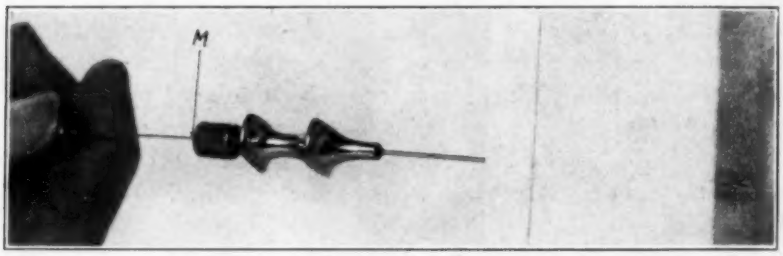

Fig. 1.—The catgut is inserted into the needle by the flat-tipped "insertion stylet," which has been pushed into the needle up to a mark (*M*) previously scored on its shaft. This mark is 3 cm. (the length of the catgut) from the end of the butt end of the stylet. The stylet is approximately the same length as the needle, and, when it is inserted into the needle as far as the mark mentioned, the catgut has been made to protrude just beyond the tip of the needle into the spinal canal.

preventing postpuncture headaches by obviating leakage of the spinal fluid after lumbar puncture. The idea underlying it was to attempt to plug the lumbar puncture needle hole in the meninges. Catgut was selected for this purpose because it is easily inserted through the needle while dry and stiff, and swells in a few minutes to twice its original diameter when wet by the spinal fluid or other tissue juices. After the experiments on dogs, which were carried on over a period of two years, had furnished satisfactory evidence that the procedure was without danger, practical application was made of it in patients.

3. Jacobaeus, H. C., and Frumerie, K.: About the Leakage of the Spinal Fluid After Lumbar Puncture and Its Treatment, Acta med. Scandinav. **58**:102, 1923.

EXPERIMENTAL STUDY

In this study, pieces of catgut of varying length were inserted at lumbar puncture into the hole left by the puncture needle in the posterior walls of the spinal canals of ten dogs. Lumbar puncture was performed in the usual way, using a 19 gage needle and inserting it no farther than the distance just necessary for the tip to enter the

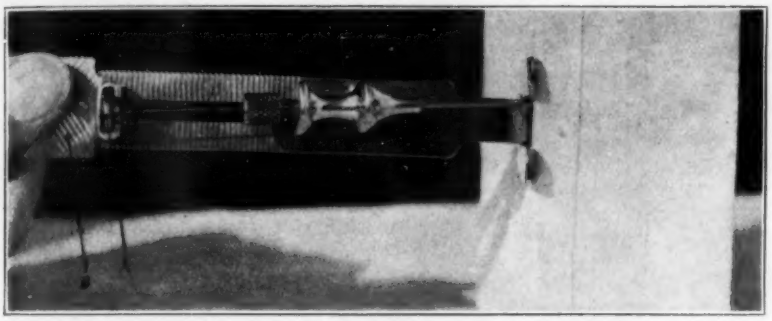

Fig. 2.—A stand with an adjustable sliding holder (*B*) is placed in position resting against the patient's back, and the button-like outer end of the stylet is placed in the holder. The corrugations on the holder fit with similar corrugations on the stand, and when the holder and stand are pressed together firmly, the button (*A*) of the stylet becomes a fixed point. In this manner the stylet and catgut are held in constant relation with the dura mater and spinal canal.

Fig. 3.—The stylet is being maintained in a fixed position by the holder, and the needle is being withdrawn, leaving the catgut (*C*) in place, protruding through the hole in the dura mater into the subarachnoid space.

spinal canal. (This point can be determined as in the human subject, by the sudden slight "give" of the needle on entering the canal.) The stylet of the needle was withdrawn and a drop or two of the spinal fluid was allowed to escape to make sure that the needle had entered the canal. Next, a special adapter for facilitating the insertion of the catgut into the spinal puncture needle was adjusted into the hub of

the needle and a piece of plain sterile catgut, previously dried to stiffness and cut with a razor to the desired length, was inserted into the hole of the adapter with the aid of flat-tipped tweezers. By means of a special stylet of measured length and flat tip, the catgut was then pushed into the needle far enough to leave its innermost end protruding just beyond the tip of the needle into the spinal canal (figs. 1 and 2). This was made possible by marking the shaft of the stylet at a distance equal to the catgut's length from its outer end and pushing

Fig. 4.—A portion of the posterior wall of the spinal canal of a dog. At postmortem lumbar puncture, it was found that a piece of catgut had been inserted into the hole left by the needle. The catgut is seen projecting about 1 cm. into the spinal canal; × 2.

the stylet into the needle up to this point. A specially constructed stand (fig. 3) with an adjustable sliding holder attached was next placed in position on the dog's back, and the button-like outer end of the stylet was fixed in the holder. The holder and stand were gripped in the left hand (fig. 4) and held firmly against the dog's back, in this way maintaining both the stylet and the catgut in a position of fixed relation with the spinal canal. The puncture needle was then with-

drawn with the right hand, leaving the piece of catgut to be held by the tissues of the lumbar region in a position filling the hole made by the needle. In these experiments, the animals were anesthetized and their backs shaved and painted with iodine before operation. Necropsies were carried out in every case and the spinal canal was examined from the level of the shoulders to the tail.

In all of the dogs, at necropsy the spinal cord was normal both macroscopically and microscopically throughout its length. In seven dogs, examined from five weeks to eleven months after operation, no trace of the catgut could be found. In two, examined three and fifteen months later, small holes were seen in the walls of the canal at the site of the puncture, and from the margin of these holes were hanging thin fibrous strands about 2 cm. in length. It could not be definitely determined whether the strands were remnants of the catgut or strips of periosteum torn loose during dissection. In one dog, which died of distemper three and a half weeks after operation, all of the six pieces of catgut that had been inserted were found projecting into the spinal canal. In this dog, as in the others, the dura and spinal cord were normal.

CLINICAL STUDY

Factors in the Causation of Postpuncture Headaches.—This study consisted in recording certain variable manifestations observed in 200 patients on whom lumbar puncture was done. Readings of pressure of the spinal fluid were taken before and after the removal of from 5 to 15 cc. of spinal fluid. Record was made also of difference in the sex, temperament (stolid or neurotic) and weight of the patients, the time required for the operation, the amount of spinal fluid withdrawn, any difficulty the needle encountered in entering the canal, the number of holes made in the dura mater and the amount of fresh blood, if any, in the spinal fluid that was removed. The last observation was made as an indication of hemorrhage set up by the needle. The measurement of the pressure of the spinal fluid was made by means of a glass L-tube manometer with a bore of 2 mm. In all cases, a 21 gage needle with a beveled point was used and the operation was done with the patients lying on their right sides. All patients were confined to bed, with heads lowered, for twenty hours or more after puncture.

Of the 200 patients in the entire series, approximately 20 per cent suffered from typical postpuncture headache. In a group of thirty patients with neurosyphilis who gave evidence of meningeal involvement, the incidence of headache was 10 per cent, or half the average. None of the other variable factors recorded, namely, the pressures of

the spinal fluid, the sex, weight and temperament of the patients, had any significant relation to the percentage of headaches that occurred after puncture.

Pressure of the Cerebrospinal Fluid Before and During Postpuncture Headache.—On three patients who were in the usual recumbent posture, pressures of spinal fluid were taken at lumbar puncture before and after the removal of 7 cc. of spinal fluid, and again, at a second puncture the next day, during typical postpuncture headache. In one of the three patients the pressure was taken in a sitting as well as in a recumbent posture, both before and during the headache (tables 1 and 2).

TABLE 1.—*Pressure of the Spinal Fluid in Two Patients, Before and During Postpuncture Headaches* *

Time of Puncture	Pressure of Spinal Fluid, C.Mm. of Water	
	First Patient	Second Patient
Before removal of 6 cc. of cerebrospinal fluid	13.0	15.0
Three minutes after removal of the cerebrospinal fluid	9.5	10.0
During postpuncture headache (next day)	2.5	2.0

* A marked fall in pressure has taken place in each case between the time of the first puncture and the time when the postpuncture headache was present.

TABLE 2.—*Pressures of Spinal Fluid in the Third Patient Punctured Before and During Postpuncture Headaches* *

Time of Puncture	Pressure of Spinal Fluid, C.Mm. of Water		Site of Puncture
	Lying on Right Side	Sitting Upright	
Before removal of 10 cc. of cerebrospinal fluid	18.0	53.0	Level of the foramen magnum
Three minutes after removal of 10 cc. of cerebrospinal fluid	11.0		
During postpuncture headache (next day)	5.5	28.0	Level of the third rib anteriorly

* The pressure was much lower during the time of the headache than it was even after removal of the spinal fluid at the time of the original puncture. There was a difference in the levels of the fluid before and during the headache when the patient was sitting upright.

Wounds in the Dura Mater and Characteristics of the Dura at the Site of Puncture.—A portion of the lumbar dura mater of a patient who had died from cerebellar tumor eleven days after spinal puncture had been performed was examined macroscopically and microscopically. Special attention was paid to the nature of the injury to the dura mater made by the puncture needle (fig. 5) and to the characteristics of the dura at the site of puncture, in order to determine how these factors might affect the possibility of leakage of spinal fluid after puncture.

Three distinct puncture wounds were found, and when first seen all were apparently closed. As shown in figures 6 and 7 the thickness

of the dura was variable; in places it was less than 0.3 mm. and in other places, more than 0.85 mm. In some regions, the dura was vascular; small vessels coursed longitudinally within it and along its walls. In other areas, it was without blood vessels. In two places, the needle had penetrated the dura almost at right angles; in the third place, it had left a tract leading diagonally through the dura. The exact points of puncture of the dura could not be located in the micro-

Fig. 5.—Wounds made in the dura mater of a patient at lumbar puncture done eleven days before death. The wounds appear to be open, owing to stretching of the specimen before it was photographed.

scopic sections, but areas of hemorrhage were found that were believed to have been adjacent to the puncture wounds.

An Attempt to Plug the Hole in the Meninges.—In the manner previously described, pieces of catgut 3 cm. long were inserted, at the time of lumbar puncture, into the hole left by the needle in the spinal meninges of 102 patients. At the same time, lumbar puncture was done, for control purposes, on ninety-two other patients, in the routine manner, without plugs of catgut. The patients on whom the catgut method

had been used were kept flat in bed for twenty hours after puncture. Those on whom puncture had been done in the customary way also were kept in bed, but with head lowered, for the same length of time.

Of the ninety-two patients used as controls, from whom spinal fluid had been removed in the ordinary manner, sixteen (17.4 per cent) had characteristic postpuncture headaches. Twenty among the ninety-two patients had had from one to fourteen previous spinal tests without postpuncture reaction. Of these twenty patients, only one suffered a reaction at the time of the test that is recorded here. Of the 102

Fig. 6.—A section of one portion of the dura mater shown in figure 5; × 100. The dura mater is 0.3 mm. thick, and blood vessels are absent.

patients in whom catgut was inserted at lumbar puncture, five (4.8 per cent) had reactions that could be interpreted as postpuncture headaches. Approximately half of the 102 patients complained of aching pains in the back, in the popliteal region and in the posterior muscles of the thighs. Twenty of the 102 patients had headaches quite different from those of typical postpuncture reactions, in that they became no worse or were definitely relieved on sitting up. These headaches first appeared while the patient was lying in bed, about twelve hours after puncture, and lasted for but a few hours, not lasting more than one day in any

case. With the patient in a horizontal position the headaches continued unabated. Three patients who had had tabetic pains previously suffered from attacks of these pains that lasted two, three and ten days, respectively, after the test was done. Seven of the 102 patients in this group were especially selected for testing the catgut method because they had had prolonged headaches following previous punctures. One patient in particular had had four previous punctures, with severe postpuncture headache lasting nine and ten days after each puncture. Of these seven patients none had postpuncture headache when the catgut plug was used.

Fig. 7.—A section of an adjacent portion of the dura mater shown in figure 6; × 100. The dura is 0.85 mm. thick, and the blood vessels are numerous.

COMMENT

The data concerning the patients on whom pressures of spinal fluid were taken before and during postpuncture headache confirm those of Jacobaeus and Frumerie and prove that between the time of spinal puncture and the onset of postpuncture headache a remarkable fall in spinal fluid pressure takes place. This fall in pressure is direct evidence of a marked reduction in the volume of spinal fluid, the cause for which, there is reason to believe, may be a leaking out of the fluid through the needle hole in the meninges.

It is apparent that the opportunity for such leakage to occur would depend on the balance of the pressures existing in the subarachnoid and epidural spaces at the needle opening. The pressure exerted by the tissues in the epidural space, at any point in the lumbar region, is in all probability determined by that of the blood in the epidural veins at that point. As assumed by Ingvar,[4] the pressure of the blood in the epidural veins at any level should, because of the anastomoses existing between the epidural and extracolumnar veins, be approximately equal to the weight of a column of blood extending vertically to the level of the mouth of the vena cava. Accordingly, the pressure of the spinal fluid that would be necessary to overcome the pressure of the tissues occupying the epidural space and cause leakage at the opening made by the needle would be that of a column of fluid reaching from the level of the opening made by the needle to a point a little above the heart. In this respect it appears to be significant that if the puncture was made with the patient in the upright position during the time of postpuncture headache, the spinal fluid rose in the manometer to the level of the heart. This suggests that at this level the pressure of the spinal fluid had been equalized by the pressure of the tissues in the epidural space and that the leakage which had occurred previously had been checked.

The pressure of the spinal fluid during postpuncture headache, in the patient just referred to, furnishes evidence that explains at least one mechanism by which postpuncture headaches are produced. As there is reason to believe that the level of fluid in the spinal subarachnoid space was at the level shown by the manometer (that is, at the level of the heart with the patient upright) it may be assumed that the spinal subarachnoid space, from the level of the heart to that of the foramen magnum, must have been virtually empty of fluid and the cranial subarachnoid space at least partly so. Under these circumstances, with the patient upright the spinal cord, no longer buoyed up by the fluid as normally, would exert downward traction equal to its weight on the brain, increasing the tendency of the brain to press against the base of the skull. This strain on the spinal cord, together with the distortion of the brain and meninges brought about by the unusual pressures acting on these structures, could hardly fail to produce severe headache. The fact that these conditions would prevail only with the patient in the upright position and that they would be mitigated immediately when the patient lay down offers the only satisfactory explanation for the constant relation of postpuncture headache to the patient's position.

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4. Ingvar, Sven: On the Danger of Leakage of the Cerebrospinal Fluid After Lumbar Puncture, Acta med. Scandinav. **58**:67, 1923.

In regard to the nature of the wounds found at necropsy in the dura mater of a patient on whom lumbar puncture previously had been done, the observations made have led me to believe that the various local differences seen to exist in adjacent portions of the meninges may have a bearing on the production of postpuncture reactions. Since the dura mater can be two or even three times as thick in some regions as in others, it is apparent that if the needle were to enter the canal through a thick portion of the dura, the chances of escape of the fluid following puncture would depend on mechanical factors quite different from those which would obtain if the needle were to make its hole in a thin portion. Where the dura is thick, it would be able to withstand considerable tension without being stretched to the point of allowing the hole to open, but where it is thin the same tension of spinal fluid might stretch it sufficiently to open the hole and allow the fluid to escape. The differences in degree of vascularity of the dura in different regions also may be of some significance. If, during puncture, the needle were to strike a vascular portion and rupture a blood vessel, bleeding would take place into the wound and help to plug it, whereas, if the needle were to penetrate the dura in an avascular portion, bleeding would not occur. The angle at which the needle pierces the dura on entering the canal likewise may affect the opportunity for subsequent leakage. If the needle were to enter the canal at right angles to the dura, leakage would be favored by the directness of the communicating passage left between the subarachnoid and epidural spaces. On the other hand, if it were to go through the dura obliquely, there would be overlapping of the edges forming the hole, following withdrawal of the needle, and a kind of valve would be formed that would have a tendency to close under pressure of the spinal fluid. It seems possible, therefore, that the opportunity for leakage to occur would depend on the particular combination of the three conditions that happened to be present at the site of puncture.

In interpreting the results of the investigations involving percentages of postpuncture reactions it is necessary to make clear what is considered a "reaction." Briefly, the distinguishing characteristics of such a reaction are that headache is usually the outstanding symptom, that it comes on when the patient assumes the upright position, that it persists for a number of days at the least, compelling the patient to remain in bed the greater part of that time, and that it disappears promptly when the patient lies down. In compiling the results of this work, only the typical reactions just described are considered.

The low incidence of postpuncture headache in patients in whom catgut was inserted at lumbar puncture supports the hypothesis that leakage is the cause of postpuncture headache. Although the figures are not conclusive, it is worth mentioning that in order to make doubly

sure no favor was being shown the method in which catgut was used, the selection of patients was purposely made in such a manner as to put the catgut method at a disadvantage in reckoning with results. Thus, the group of ninety-two patients on whom spinal puncture was done without catgut included twenty who had had from one to eleven previous punctures without headache, whereas the group of 102 patients on whom it was done with catgut included none of this type. On the other hand, the latter group did include all seven patients who had suffered from postpuncture headaches previously, and none of these seven patients had postpuncture headache following the use of catgut.

SUMMARY

Readings of pressure of spinal fluid were taken on 200 patients before and after removal of from 5 to 15 cc. of spinal fluid. Records were also made of the following: (1) differences in patients with respect to sex, weight and temperament, (2) the amount of fluid withdrawn, (3) time required for the operation, (4) difficulty of inserting the needle in the canal, (5) the number of wounds made in the dura and (6) the presence or absence of fresh blood in the fluid that was removed. Typical postpuncture reactions occurred in approximately 20 per cent of these patients. There did not appear to be any relation between pressures of spinal fluid or any of the conditions mentioned and the incidence of headache.

Readings of pressure of spinal fluid were taken on three patients before and after removal of 8 cc. of spinal fluid, and again the next day, during typical postpuncture reactions. In all three patients, the pressure was found to be remarkably low during the headache, indicating a great reduction in the volume of spinal fluid in the spinal subarachnoid space. In one patient, in the sitting posture, before the headache appeared the fluid rose in the manometer to the level of the foramen magnum as in normal persons, and during the headache to the level of the heart. This is of apparent significance in relation to the theory of leakage as a cause of postpuncture headache.

A portion of dura mater was removed at necropsy from the lumbar region of a patient, eleven days after spinal puncture had been done. Three wounds of puncture were seen in the dura. It was found that the dura varied in thickness in different regions, that it was vascular in some places and avascular in others and that the needle had penetrated the dura in two of the wounds at right angles and in the third, obliquely. It is believed that such variable factors may operate either to favor or to prevent leakage of spinal fluid following lumbar puncture.

In ten dogs, pieces of catgut were inserted, at lumbar puncture, into the tracts left by the needles in the lumbar tissues and in the walls

of the spinal canals. The catgut disappeared in from four to five weeks. The spinal cord and the meninges were not injured by the procedure.

In 102 patients, pieces of catgut 3 cm. long were inserted at lumbar puncture in the hole left in the meninges by the puncture needle. Five of the patients (4.9 per cent) had typical postpuncture reactions. Sixteen (17.4 per cent) of ninety-two patients on whom ordinary spinal puncture was concurrently done suffered from typical postpuncture reactions. It is believed that in the first group of patients the catgut aided in preventing postpuncture headache by plugging the hole that remained in the meninges after puncture.

PRIMARY SYPHILIS OF THE CERVIX UTERI*

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A history of syphilis in women is difficult to obtain. The existence of a latent syphilis is frequently brought to light by a stillbirth, or by the birth of a living infant with all the stigmas and characteristic evidence, both clinical and laboratory, of congenital syphilis.

Wile and Senear [1] state, for obvious anatomic reasons, that the primary syphilitic sore in women is apt to remain a hidden and unrecognized lesion. The knowledge that the primary lesion of syphilis on the genitalia of women is extremely transitory dates back to the teachings of Fournier.[2] The American literature concerning chancre of the cervix is not extensive; Gellhorn,[3] Wile and Senear,[1] Gellhorn and Ehrenfest,[4] Warthin and Noland,[5] Stookey,[6] and MacDonald,[7] all contributed to a comparatively scanty literature on the subject. Gellhorn and Ehrenfest [4] in their first contribution placed the incidence of chancre of the cervix at less than 10 per cent of all primary manifestations of syphilis in women. In a subsequent communication, Gellhorn [3] stated that he believed the incidence was greater. The dispensary clinician, who has the opportunity to see a large number of cases of early cutaneous syphilis in women, is impressed by the large percentage of cases in which the primary lesion of syphilis, with its associated satellite bubo, cannot be found. The teachings of Fournier, then, must be accepted as to the transitory nature of the primary lesions of syphilis in women, and it must be assumed that the chancre and its associated bubo have resolved before the cutaneous manifestations develop. In my judgment, this would be an improbable assumption, when one con-

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1. Wile, U. J., and Senear, Francis: Chancre of the Cervix Uteri, Surg. Gynec. Obst. **21**:643 (Nov.) 1915.

2. Fournier, quoted by Shillitoe, Arthur, in Power, D'Arcy: System of Syphilis, New York, Oxford Med. Pub., 1908, vol. 1, p. 239.

3. Gellhorn, George: Syphilis of the Cervix, J. A. M. A. **87**:1812 (Nov. 27) 1926.

4. Gellhorn, George, and Ehrenfest, H.: Am. J. Obst. & Gynec. **73**:864, 1916.

5. Warthin, A. S., and Noland, L.: Differential Diagnosis of Chancre of the Cervix and Carcinoma of the Cervix, Am. J. Syph. **5**:553 (Oct. 21) 1921.

6. Stookey, P. F.: Primary Manifestations of Early Syphilitic Lesions of the Cervix, Am. J. Syph. **2**:68 (Jan.) 1927.

7. MacDonald, Carolyn V.: Early Syphilitic Lesions of the Cervix, J. A. M. A. **92**:662 (Feb. 23) 1929.

siders the indolent character of the syphilitic bubo of the inguinal glands in untreated chancre of the labia. The alternate assumption that the chancre was hidden for anatomic reasons and that the associated bubo is present in the deep glands of the pelvis is to my mind by far the most reasonable assumption.

During the past three years in the syphilis clinic of the Kansas City General Hospital, all women with early secondary cutaneous syphilis have been subjected to examination of the cervix. As a result, chancre

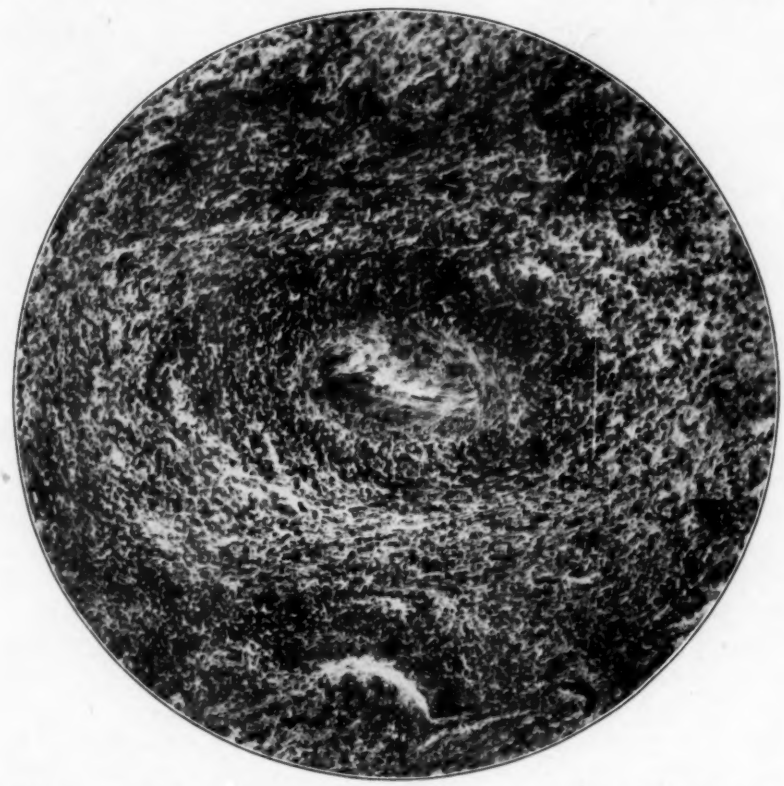

Fig. 1.—The center of the section is occupied by arteries which show a collapsed lumen. The muscle fibers of these arteries are apparently normal. The arteries here are infiltrated and not sharply outlined. There is a definite cellular infiltration around the blood vessels. This infiltrate consists of round cells which under the high power show mostly plasma cells, fewer lymphocytes, and few leukocytes. The surrounding tissue consists of fibrous tissue in circular arrangement. In the fibrous tissue is a dense infiltrate of the same type of cells, mostly arranged in columns. There are many capillaries with large cells on their walls. The endothelial cells are increased in number and partly obstruct the lumen. This microphotograph was made from deep beneath the epithelium and the entire cervix shows the same pathologic change. This histologic report is given by the courtesy of Dr. Robert Koritschoner, consulting pathologist, Kansas City General Hospital.

of the cervix has been diagnosed in forty-two instances. These forty-two cases form the basis of this report. In all of these cases, the early cutaneous eruption was present, associated with a positive blood Wassermann reaction; the satellite bubo was absent. The dark-field examination was repeatedly positive for motile *Spirochaeta pallida*. It has been established [5] that the cervical secretion from the normal cervix in a woman suffering from early secondary syphilis with the primary lesion

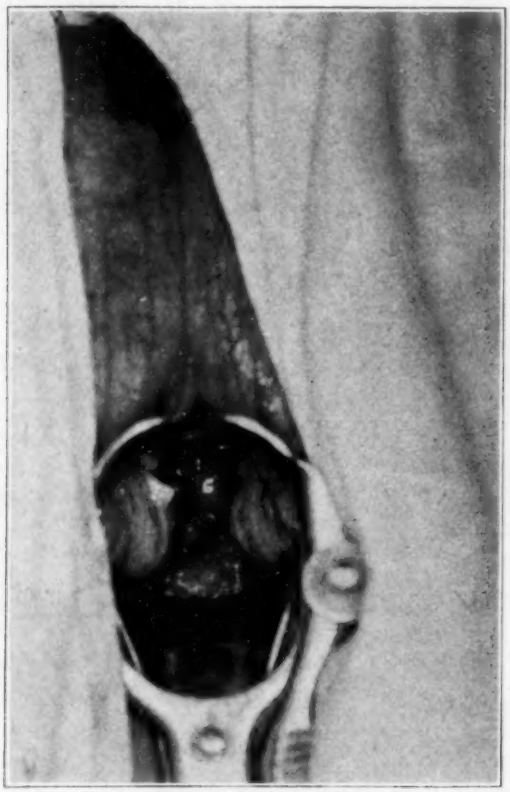

Fig. 2.—L. D., a multipara, aged 30, entered the hospital because of intense headache. Physical examination was negative aside from the appearance of the cervix shown here. A tentative diagnosis of carcinoma was made and biopsy done. Three days subsequent to biopsy, typical early macular cutaneous manifestations of syphilis appeared.

on the labia will occasionally show *Spirochaeta pallida* on dark-field examination. To guard against this remote possibility of error, the material utilized for dark-field examination was obtained from the cervix after a preliminary cleansing of the mucosa. Subsequently the mucosa was irritated, and the serum that exuded from beneath the mucosa was collected for examination. It was found that when a cervix

was the seat of a chancre, a positive dark-field could be obtained anywhere from the cervical mucosa. This fact is in accord with the biopsy results, which generally show a diffuse round cell infiltration encircling the entire circumference of the cervix in contrast to the circumscribed character of initial lesions as typified by the classic hunterian sore in the male.

The anastomosis between the parametrial glands and the inguinal glands may give rise to an enlargement of the inguinal glands, even if the cervix is the site of the chancre. Fortunately this confusing fact is exceptionally encountered, and in my experience, the response of the inguinal glands has not been so marked as in the true satellite bubo.

The appearance of primary syphilis on the cervix is entirely foreign to the classic conception of the hunterian sore. In their cases, two of which were described in detail, Wile and Senear [1] drew graphic pictures of the chancre with its associated edema. The most striking observation in my series of cases was the extreme edema. It is obvious that preexisting pathologic conditions and concurrent infections will influence the clinical picture. Coexisting gonorrheal infections, infections from previous septic abortions and lacerations from previous labors all form a part of the pathologic process. Induration, which is of such extreme clinical significance in primary syphilis in the male, is, in my experience, present in less than 10 per cent of all cases. The clinical impression from inspection is the extreme degree of edema present; to the gloved examining finger, the lesions are soft and boggy. These descriptive terms are used in comparison with the feel of the normal cervix.

The so-called diphtheroid type of chancre that is occasionally encountered bleeds on the least provocation. The pseudomembrane may be extensive. In two cases of the diphtheroid type, Vincent's organism, with its associated spirochete, was encountered. It is generally accepted that Vincent's organisms occur around the clitoris, and that the cervix in health, is free from these saprophytic organisms. In both of the cases, in which Vincent's organisms were recovered, there was a coexisting gonorrheal infection of the endocervical glands. Carcinoma is closely simulated, and a large fungating mass, which is friable and bleeds on manipulation, may present itself when the speculum is introduced. The syphilitic nature of the lesion may be assumed if the dark-field is positive, and regression occurs under antisyphilitic therapy. Biopsy is the most satisfactory procedure to establish the diagnosis definitely. Destructive ulceration was not encountered. Erosions and extremely minute superficial ulcerations are present in a majority of cases. Exceptionally, these ulcerations carried the impression of primary syphilis, but as a general rule they were of little clinical significance.

The most astounding group of initial lesions encountered in this series of cases was the cervix that presented no visible evidence of disease aside from marked edema. The enlargement was extreme, the cervix being three or four times the normal size. To the gloved examining finger the lesions were soft and doughy in consistency, and absolutely free from all suggestion of induration. It is my impression that this manifestation of primary syphilis occurs when the previously normal cervix is invaded by *Spirochaeta pallida.*

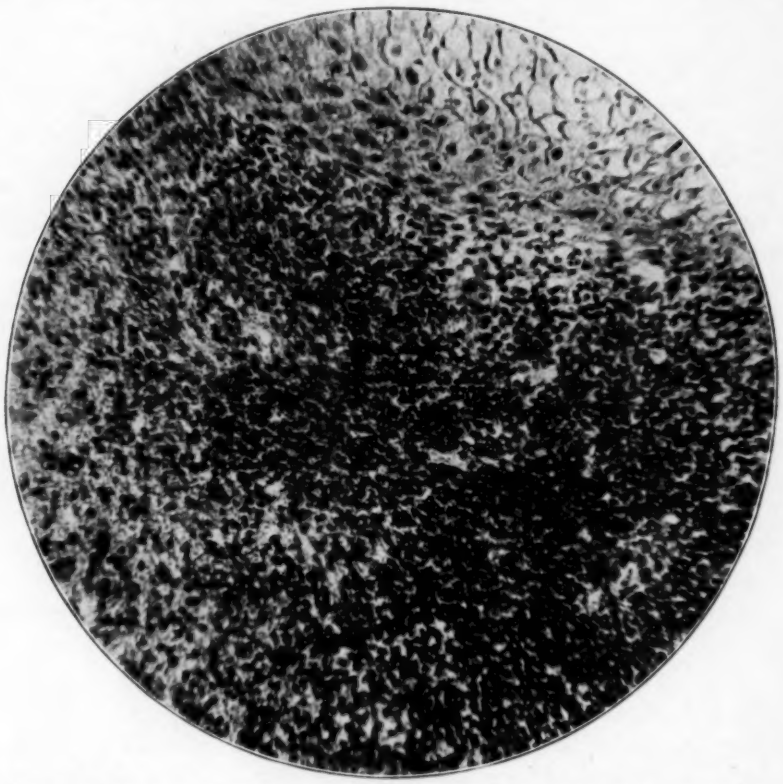

Fig. 3.—This photomicrograph was taken near the surface of the epithelium of the cervix. The pathologic changes extend somewhat into the deeper layers of the tissue on each side, and to the proximal part of the cervix. The outstanding feature is the dense infiltration of round cells that consist partly of plasma cells and partly of lymphocytes. The blood vessels show enlargement of the nuclei of the wall, and enlargement and increased number of endothelial cells which partly obstruct the lumen. The epithelium itself shows a vacuolation of the cytoplasm cells. There are a few round cells migrating into the epithelium. This histologic report is given by courtesy of Dr. Robert Koritschoner, consulting pathologist, Kansas City General Hospital.

In the series of cases under discussion, constitutional syphilis was present in all cases, and the attempt to locate the initial lesion led to complete, and at times, tedious examination of every cervix.

In the absence of constitutional symptoms, associated with a negative serology, the diagnosis of syphilis must be established from the cervix alone. Such a diagnosis can be established only by a positive dark-field, or by biopsy. The only working rule that I could formulate is that every cervix that presents marked edema should be looked on with suspicion, and an attempt should be made to establish a definite diagnosis of syphilis by laboratory procedure. Wile [8] cautioned physicians against errors of tradition. The idea of the transitory character of the mani-

Fig. 4.—L. W., a woman, aged 24, had a macular eruption over the abdomen, and over the flexor surfaces of the extremities. A satellite bubo was absent. The cervix was large and edematous, and presented numerous extremely small ulcers. Dark-field examination from cervix was repeatedly positive. Wassermann reaction was four plus.

festations of syphilis on the genitalia of women is, in my judgment, an error of tradition. Mucous patches heal as rapidly in the male as in the female, whereas condylomata lata are slow in their evolution in both

8. Wile, U. J.: Perpetuation of Error in Dermatology, J. A. M. A. **91**:219 (July 28) 1928.

sexes. Cold or indurated edema responds slowly to treatment. In cases in which the primary syphilis with edema is associated with an endocervicitis, it is difficult to separate the pathologic reaction by the invaded tissue. The cold edema, so often a complication of primary syphilis of the female genitalia, frequently gives a marked Herxheimer reaction. The wide diversity of description that occurs in the literature of the clinical appearance of chancre of the cervix can be interpreted only as absolute evidence that primary syphilis of the cervix is extremely protean in its manifestations.

SUMMARY

The cervix is a common site of the primary manifestation of syphilis. Early secondary syphilis, manifest in the skin and lymph glands, with an absence of the satellite bubo, is strong presumptive evidence that the cervix is the port of entry for *Spirochaeta pallida*. Edema, with or without ulcerations, is the clinical manifestation of chancre of the cervix. The initial lesion of syphilis may occur on the cervix, and the only tissue reaction resulting will be an extreme edema. Diagnosis can be definitely established only by examination of the dark-field or by biopsy.

ABSTRACT OF DISCUSSION

DR. WILE, Ann Arbor, Mich: The subject of chancre of the cervix has always interested me, and I was glad to hear Dr. Stookey discuss it again. As early as 1915, Dr. Senear and I [1] called attention to apparently occult infection in women, in which we established the cervix as a site of the initial infection. We directed attention at that time to the fact that cervical chancre was undoubtedly far more common than is generally accepted, because it is infrequently looked for. I find myself, therefore, entirely in accord with the speaker's view that it is a common site of infection in women. With regard to the type of chancre which is present, I believe that it is usually seen as a flat, purplish erosion, somewhat sharply raised from the surrounding tissue, and not infrequently covered by a pseudomembranous exudate. The lower lip is more frequently involved than the upper, but as in the rectum and urethra, the lesion may be linear, and extend up to the cervical canal. I have also seen a hypertrophic fungating vegetative lesion on the cervix which was apparently the primary sore. The edema that Dr. Stookey called to our attention touches, I believe, on an important differential diagnostic point. However, many cervical chancres, particularly in nonparous women, occur without edema and merely as circumscribed erosions, the induration of which is difficult to determine, because of the normal resilient quality of the nonparous cervix. The only part of Dr. Stookey's description to which I cannot entirely subscribe, is the third variety which he describes, in which there is but little present except a large, edematous cervix without solution of continuity of the mucous membranes, on which apparently he bases a diagnosis of primary sore on the presence of spirochetes. While it may be possible that these edematous lesions are true primary infections, it would seem to me difficult to rule out the possibility that they represent deep-seated, turgid secondary lesions. Particularly is this a possibility when one realizes that, during the exanthematous period, edema of the genitalia is not at all uncommon. Still, a last minor point to which exception might be

taken is the statement that it is a traditional error that the primary and secondary lesions occurring on the genitalia of women are transitory. As the author stated, this statement was made originally by Fournier, and in my experience it is true. The differences in anatomic structure of the external genitalia in women, and their greater degree of vascularity, I think explain quite readily the more effervescent character of early lesions in women than in men. For this reason, of course, such lesions are the more dangerous in their difficulty of detection, and have a greater tendency to recurrence when untreated. The investigation of the subject by those who are not familiar with the clinical picture is well worth while, and it is timely to have attention called to it.

Dr. Dennie, Kansas City, Mo.: I have been fortunate in seeing most of these cases with Dr. Stookey, and the thing that impressed me the most was the marked enlargement of the cervix. When the speculum was introduced, the cervix completely filled it. Two or three weeks after treatment had been instituted, the cervix was reduced in size, showing that antisyphilitic treatment had reduced it to normal. It is true not only that primary syphilis enlarges the cervix, but also that tertiary syphilis does. Women whom I have treated for primary syphilis have reported at the clinic with enlargement of the cervix and with ulceration extending into the canal. This condition disappeared in from three to six weeks after treatment with potassium iodide, however, leaving a thin scar at the cervix. These lesions are not chancre redux. As Dr. Wile stated, this condition is practically unknown to gynecologists. I think every lesion of the cervix should be subjected to careful dark-field examination in order to determine whether or not it is syphilitic.

Professor Jadassohn, Breslau, Germany: It is necessary to examine microscopically all clinically found lesions. In all cases of women who have been exposed to syphilitic infection one must also make microscopic examinations of the secretion of the cervical canal and of the urethra. That this is necessary has been proved by the experiments of my assistants, Miss Fuchs and Miss Trost. We tell all male patients who come to the polyclinic, with recent syphilis, to send also the women with whom they have had contact. We examined all of those women. Sometimes we find clinical symptoms in the vulva or on the portio. Often we find no symptoms when the Wassermann reaction is positive. In a number of cases we find that clinically these women are quite normal, but when we make preparations from the secretion of the cervical canal and of the urethra we find *Spirochaeta pallida* in a typical manner. Sometimes it is necessary to make as many as eight preparations of the cervical canal. When a woman has been exposed to infection by a man with recent syphilis some of us say these women will surely be infected and that they be treated. Others say one must wait, examining patients frequently, until one finds either *Spirochaeta*, syphilitic lesions or a positive Wassermann reaction. Treatment then must begin, but not before, according to the general rule that it is always advisable to give no treatment before having exhausted all diagnostic measures.

In my series of cases there were some women who had had sexual contact with men with recent syphilis, having lesions on the genitalia. These women were examined in every way, and in some treatment was not instituted, even though the physicians who represent the first group made the examination of the cervical and urethral secretions, because no *Spirochaeta* or other evidence of syphilis was found. The cases were followed up for a long time and reaction remained negative. This proves that not all of the women who have contact with men with contagious symptoms of recent syphilis on the genitalia must necessarily become infected.

DR. CANNON, New York: Dr. Stookey's paper is of tremendous importance in presenting the characteristic appearances of the initial genital lesion in women. Our experience at the City Hospital has shown us that in fully 99 per cent of the women admitted there from houses of correction for the treatment of syphilis the disease had not been recognized by the examining physicians until there were evidences of secondary lesions, or positive Wassermann reactions. I am sure it would greatly decrease the spread of syphilis and aid us in our cure of the disease if physicians were able to recognize the chancre in women and would make a satisfactory vaginal examination.

DR. STOOKEY, Kansas City, Mo.: The recognition of chancre on the cervix, in my judgment, can be accomplished only by laboratory procedure, the dark-field examination or biopsy. I have visited several local gynecologic clinics in an attempt to recognize these lesions before the development of the cutaneous eruption, and am rather doubtful that any one can recognize them without the assistance of the laboratory.

BERLOCK DERMATITIS

UNUSUAL DERMATITIS AND PIGMENTATION FOLLOWING USE OF PERFUME *

PAUL GROSS, M.D.
AND
LEWIS BYRNE ROBINSON, M.D.
NEW YORK

For a number of years we have been familiar with the literature concerning a curious pigmentation of the skin, originally described by Freund,[1] in 1916, and later named Berlock dermatitis by Rosenthal.[2] This condition results from the application of toilet waters to the skin immediately before it is exposed to the sunlight.

During the early part of the summer of 1929, we had our first occasion to observe an actual case, following this, four other cases were seen within a short period of time. The question arises as to whether it was a mere coincidence that this number of cases had been seen in such an unexpected manner. Since this is the first report of such a condition in the United States, we shall review briefly the literature and also present our conception of this dermatitis.

In 1916, Freund, in Triest, at Unna's request published reports of a series of cases observed during the summer of 1914. Apparently these observations were forgotten until 1924, when Franz Rosenthal again presented similar cases before the Berlin Dermatological Society. Following this, Hoffmann and Schmitz [3] published reports of another series of cases. Since that time similar reports have appeared from Germany, Austria, France, Italy and Czechoslovakia. It is of interest to note that Urbach [4] of Vienna obtained a typical Berlock dermatitis after removing the marks of an indelible pencil from the skin by means of benzine; also, that Zurhelle [5] considered that perspiration, in conjunction with the other causative agents, is a factor in the production of the dermatitis.

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* Submitted for publication, Sept. 19, 1929.

* From the Department of Dermatology, Vanderbilt Clinic, College of Physicians and Surgeons, Columbia University.

1. Freund: Dermat. Wchnschr. **63**:931, 1916.
2. Rosenthal, F.: Zentralbl. f. Haut- u. Geschlechtskr. **13**:322, 1924.
3. Hoffmann and Schmitz: München. med. Wchnschr. **72**:1414, 1925.
4. Urbach: Zentralbl. f. Haut-u. Geschlechtskr. **28**:451, 1928.
5. Zurhelle: Zentralbl. f. Haut-u. Geschlechtskr. **28**:404, 1928.

However, except for some experimental work by Zurhelle and Szántó,[6] little has been added to the first observations made by Freund. He originally described a pigmentation of peculiar shape that suggested its artificial cause. Such pigmentation occurred in both men and women who had been exposed to intense sunlight while bathing. In all of these cases the patients had applied eau de cologne (Atkinson) to the areas subsequently pigmented and had then immediately been exposed to sunlight. Freund furthermore succeeded in reproducing the pigmentation by applying eau de cologne and also oil of Bergamot, which is one of the essential oils in this toilet water. He even at that time tried to use the photosensitizing properties of the toilet water to tan areas of vitiligo.

In the cases reported by us, no eau de cologne was used. The agent was perfume, applied by daubing the stopper of the perfume bottle, according to feminine custom, on the ears, the neck and the axillae. It is also notable that in all five cases reported the patients used one brand or another of a well known imported perfume designated here as G. M. and G. S.

REPORT OF CASES

CASE 1.—In the beginning of June, a red spot developed rather suddenly on the side of Mrs. A. F.'s neck; after several days, this spot changed into a brownish area of pigmentation. She had used no eau de cologne, but she said that she had applied G. S. perfume with a stopper, and had immediately gone out on the golf course and into strong sunlight.

On the right side of the neck was a pear-shaped area of pigmentation, the tip pointing downward. This area was, roughly, about the size of a dollar and was brown with a slight mottling of dark red, most noticeable along the periphery.

CASE 2.—Miss B. (fig. 1, photographed on June 5) had noticed two red spots—one on the upper part of the chest, and one behind her right ear. She remembered applying perfume (G. M.) on May 29 and on May 30 and then sitting in sunlight for several hours.

On the part of the neck next to the occipital hair line was a patch the size of a half dollar. It was light brown and in places was mottled with red. Another oval-shaped distinctly red spot free from any scales was present on the chest below the right sternoclavicular joint.

CASE 3.—Miss K., on June 5, 1929, showed spots on her neck. They appeared about Easter after she had spent a few days in Atlantic City. She had the same condition in 1926 while she was in the West Indies. She had been in the habit of applying perfume (G. S., etc.) on the neck and behind the ears.

On the right side of her neck was a streak of grayish brown about four inches long and a fourth of an inch wide. She had similar patches of irregular bizarre outline on the back of the neck and on the chest.

CASE 4.—Miss F. L. was seen in our office on June 7, 1929. She had applied G. S. to her neck and chest several days before and then had immediately gone out into the sunshine.

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6. Szántó, Jeno: Orvosi hetil. **72**:839, 1928; abstr., Zentralbl. f. Hauts-u. Geschlechtskr. **28**:451, 1928.

On the side of the neck and on the upper part of the chest were scattered about a dozen sharply bordered, red, nonscaling areas of pigmentation.

Last year, the patient's sister came to the office for advice concerning a similar dermatitis which we did not at the time recognize as Berlock dermatitis.

CASE 5.—Mrs. R. C. seen on July 5, 1929, about two weeks before had noticed a brownish discoloration in the anterior axillary folds. When questioned, she said that she used a G. M. perfume but not under the arms. She had been applying odorono to her armpits and G. M. perfume on her dress, especially around the armpits.

On the anterior axillary fold, more marked on the left than on the right side, was a café au lait colored pigmentation that had a sharp border toward the chest and did not extend into the axilla.

EXPERIMENTAL WORK

Test A.—This test was made in case 2. A drop of the perfume (G. M.) was applied to the patient's back. The perfume was applied in the cut-out center of a piece of paper similar to the shape often seen in this dermatitis. The entire back was

Fig. 1 (case 2).—Pigmentation on the back of the neck, following application of perfume.

then exposed to a suberythema dose of rays produced by the air-cooled quartz light. Three days later a dark red erythema, as shown in figure 1, appeared on the spot where the perfume had been applied. The skin on the rest of the exposed back did not give any reaction to the Alpine rays. Some pigmentation still remained eight weeks later.

Test B.—A similar test was made in case 3, but the patient failed to report for observation.

Test C.—A test was made on a patient with vitiligo. Perfume was applied to the normal skin in the lumbar region (G. M. and G. S. and also eau de cologne). The back was exposed to a suberythema dose of Alpine rays. No redness or erythema appeared at the site of application of the perfume.

Test D.—The patient had normal fair skin. We applied perfume (G. M. and G. S.) and odorono after which her back was exposed to the Alpine rays. On the second day, a mild sun erythema appeared over the entire back except in areas to which the aforenamed agents were applied; here the skin remained a normal white. In this case the perfume apparently acted as a filter on the site of application, as mentioned by Sźantó in a recent article.

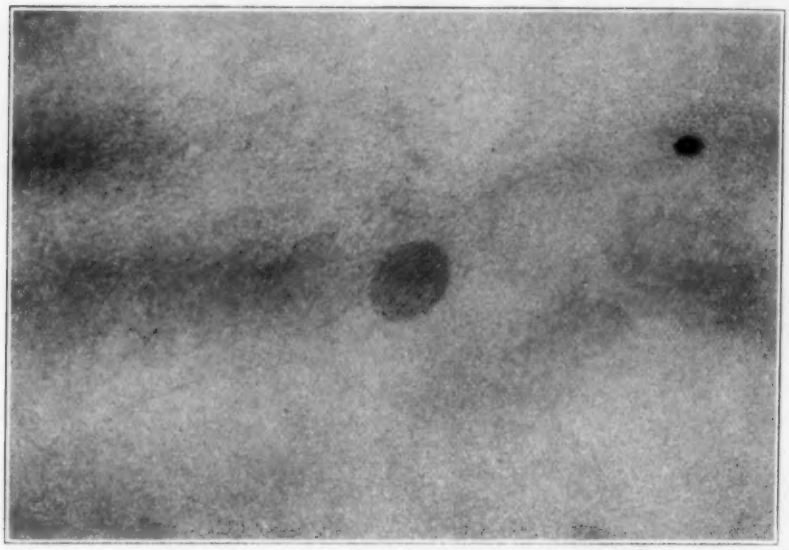

Fig. 2 (case 2).—Area of pigmented dermatitis showing a shape seen frequently in Berlock dermatitis.

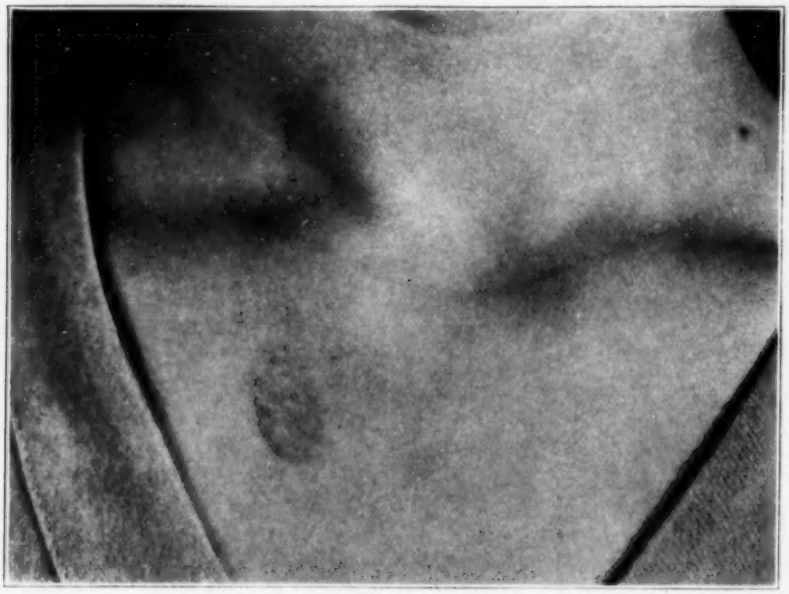

Fig. 3 (case 2).—Dermatitis artificially produced by means of perfume and Alpine light.

In our observations of cases and those reported in the literature, this dermatitis has definite characteristics. It is usually found on the neck and chest, and appears as dark red areas changing to brown slightly mottled with red. The shape of such an area is usually similar to that of an area covered by a small drop of flowing fluid, and it generally appears during the summer.

The question arises as to whether one is dealing with a personal susceptibility or with several factors, such as climate, perspiration, brand of perfume and short intervals between application of inciting cause and exposures to sunlight.

In view of the fact that perfumes and toilet waters are so widely used and that sunbaths have become so popular, we are inclined to think that there must be some predisposing factor. The number of cases seen and the number of people under the conditions seeming to cause this dermatitis are not in proportion. The few tests made tend to support our conclusion. However, this conception does not conform with the conclusions of Sźantó, who in his work made a long series of exact tests.

We have started experimental work on a larger scale, the results of which will be published later, with the idea of determining the actual causative factors in Berlock dermatitis.

FAMILIAL XANTHOMA*

UDO J. WILE, M.D.
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AND
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A careful review of the literature revealed fourteen instances of xanthomas involving members of the same family. This number comprised a total of forty-two patients. It is permissible, therefore, to class cases of familial xanthomas among the rarities and add them to the cases previously recorded.

Attention was first called to familial cases of xanthoma, in 1889, by Ehrmann,[1] and Lehzen and Knauss.[2] Ehrmann's cases occurred in two brothers, aged 7 and 9 years, respectively. In both, the eruption began when the brothers were aged 5 years, and was present over the elbows and buttocks.

Lehzen and Knauss reported the case of a girl, aged 11 years, who presented both xanthomas and xanthelasmas. The eruption first made its appearance when the patient was 4 years of age. Her sister, aged 9 years, presented an identical eruption, which made its appearance when she was 3 years old. The older girl had a mitral insufficiency, which, as the postmortem examination showed, was due to xanthomas of the endocardium.

In 1894, Thibierge reported two cases of xanthomas in brothers, aged 18 and 20. In the younger one, the lesions appeared when he was 14 years old, and in the older one when he was 8 years.

Leskien,[4] in an inaugural dissertation in 1903, reported three cases of xanthomas occurring in children of the same family. Two boys, aged 9 and 12 years, and one girl, aged 6 years, were afflicted. The parents and one other child were free from symptoms. In addition to xanthomas, the two boys also had xanthelasmas, and the lesions in all three patients had an identical distribution. In the boys, the eruption

* Submitted for publication, Sept. 23, 1929.

* Studies and Contributions of the Department of Dermatology and Syphilology, University of Michigan Medical School.

1. Ehrmann: Beitr. z. klin. Chir. **4**:341, 1889.
2. Lehzen and Knauss: Virchows Arch. f. path. Anat. **116**:84, 1889.
3. Thibierge: Ann. de dermat. et syph. **5**:318, 1894.
4. Leskien: Inaugural Dissertation, Leipzig, 1903.

first made its appearance when the younger was 7 years of age and the older 8 years. In the girl, the lesions first appeared when she was 5 years of age, and were not yet as widely distributed as in the boys.

Gwynne,[5] in 1905, reported the cases of two brothers who presented xanthomas with a similar distribution in both cases. The older brother, aged 10 years, died suddenly, but no autopsy was performed. The younger one had a mitral systolic murmur, and at one time had been jaundiced. There was no evidence of diabetes in either patient.

In 1910, Arning[6] reported a most unusual instance of familial xanthoma. The eruption was present in the mother and in four of nine children. It was further worthy of note that all these patients had heart lesions, but none of them had glycosuria or was ever jaundiced.

In 1920, Linser[7] reported the case of a family of five children in which four were afflicted with xanthomas. In each child, the eruption appeared when the patient was 5 years of age. The parents were not afflicted.

Two years later, Schmidt[8] reported the cases in this family more in detail. He stated that of the four children involved, three were girls. In the oldest, aged 15 years, the eruption appeared when the patient was 3½ years of age. In a younger sister, aged 9 years, the eruption appeared when she was aged 5 years, and in the youngest when she was 6 years of age. In the brother, aged 13 years, the eruption first made its appearance at the age of 3 years.

Beeson and Albrecht[9] reported typical xanthomas in a man whose mother had yellowish patches on both upper eyelids, but none elsewhere. He had two brothers who had skin lesions similar to his own, but not so numerous or so well developed. One brother, aged 24, had yellowish growths below the eyes, on the hands, knees, elbows and buttocks. Another brother, aged 32, had similar tumors below both eyes, over the knees and on the right hand. Two other brothers and two sisters had no skin lesions. No member of the family had ever had jaundice or diabetes.

Pautrier and Levy[10] reported a series of three cases of xanthoma in the same family. These authors were interested chiefly in the mechanism of the formation of the tumors and their histopathology.

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5. Gwynne: Rep. Soc. Study Dis. Child. **5**:318, 1905.
6. Arning: Arch. f. Dermat. u. Syph. **105**:290, 1910.
7. Linser: München. med. Wchnschr. **67**:85, 1920.
8. Schmidt: Arch. f. Dermat. u. Syph. **140**:408, 1922.
9. Beeson, B. B., and Albrecht, P. G.: Contribution to Study of Xanthoma Tuberosum, Arch. Dermat. & Syph. **8**:695 (Nov.) 1923.
10. Pautrier and Levy: Presse méd. **31**:728 (Aug. 22) 1923.

In 1924, Gordon and Feldman [11] reported the case of a man, aged 40, who presented multiple xanthomas and glycosuria. His mother was said to be similarly afflicted, and one sister had diabetes, but no xanthomas. When the patient was on a diabetic diet, the xanthomas involuted, only to recur again when the diet was relaxed.

Hufschmitt,[12] in 1924, recorded the case of a young man, aged 17 years, who presented multiple xanthomas, and in whom the eruption appeared when he was 10 years old. Three sisters presented similar lesions, while one brother was free from them.

Gilbert, Chabrol and Benard [13] reported the case of a young man, aged 18, who presented both xanthomas and xanthelasmas. Two of his brothers and two cousins were similarly afflicted, and in all the eruption first made its appearance when they were 4 years of age. These patients were members of a xanthelasmic family, in which exanthelasmas and occasional xanthomas were present in four generations. The grandmother and great aunt were spared.

As members of the xanthoma commission appointed by the Pathological Society of London, Hutchinson, Sangster, and Crocker collected several cases of familial xanthomas. One of these, that of a man aged 45, who presented typical xanthomas, was reported to them by Mackenzie.[14] One of the patient's brothers and one sister were also affected, and the paternal grandfather had a similar eruption.

Startin [15] recorded the cases of a girl, aged 5 years, and of her brother, aged 6 years, who presented typical xanthomas. The parents were healthy and unaffected. The cases were also reviewed and accepted by the xanthoma commission.

MacDonagh [16] recorded an unusual case of xanthoma in a 5 months old infant. The lesions were first noticed fourteen days after birth. The mother said that she was born with a similar eruption, which persisted until her fourteenth year, and then disappeared spontaneously.

There are on record several other cases of xanthomas affecting one member of a family and xanthelasmas another, notably those reported by Harbitz [17] and McMurray.[18] Many cases reported as xanthomas

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11. Gordon, W. H., and Feldman, M. S.: Xanthoma Diabeticorum: Question Familial Tendency, J. Michigan M. Soc. **23**:231 (June) 1924.

12. Hufschmitt: Presse méd. **32**:99 (Jan. 30) 1924.

13. Gilbert, Chabrol and Benard: Bull. et mém. Soc. méd. d. hôp. de Paris **22**:1067, 1926.

14. Mackenzie: Tr. Path. Soc. London **33**:370, 1882.

15. Startin: Tr. Path. Soc. London **33**:373, 1882.

16. MacDonagh, quoted from Arzt: Arch. f. Dermat. u. Syph. **126**:809, 1919.

17. Harbitz: Tumors of Tendon Sheaths, Joint Capsules and Multiple Xanthomas, Arch. Path. **4**:507 (Oct.) 1927.

18. McMurray: M. J. Australia **1**:528, 1920.

have been purposely omitted, and only those included which either clinically or histologically conform to the opinion of Pollitzer,[19] who first gave an accurate description of, and pointed out the difference between, xanthoma and xanthelasma.

Grenaud,[20] in a review of cases of xanthoma, reported that these conditions occurred about equally in both sexes, and that the age of the patients on the appearance of the lesions varied between birth and 40 years, with the greatest number beginning in patients between 3 and 6 years of age.

In the cases herein reviewed, the age of the patients when the lesions appeared varied between 14 days and 14 years. In the greatest number of cases, the lesions were first noticed when the patients were between 3 and 6 years of age. Seven patients gave evidence of visceral involvement, one exhibiting jaundice and six cardiac lesions. It is of more than passing interest that in all the cases showing cardiac involvement, the mitral valve alone was attacked. Glycosuria was present in only one instance, and this patient had true diabetes. Ten patients had xanthelasmas as well as xanthomas. The sex is not given in all the cases recorded, but in those in which it was, approximately an equal number of each sex is seen to be afflicted. Hypercholesterolemia was noted in only three patients, but in most of the cases reviewed blood chemical studies were not done.

REPORT OF CASES

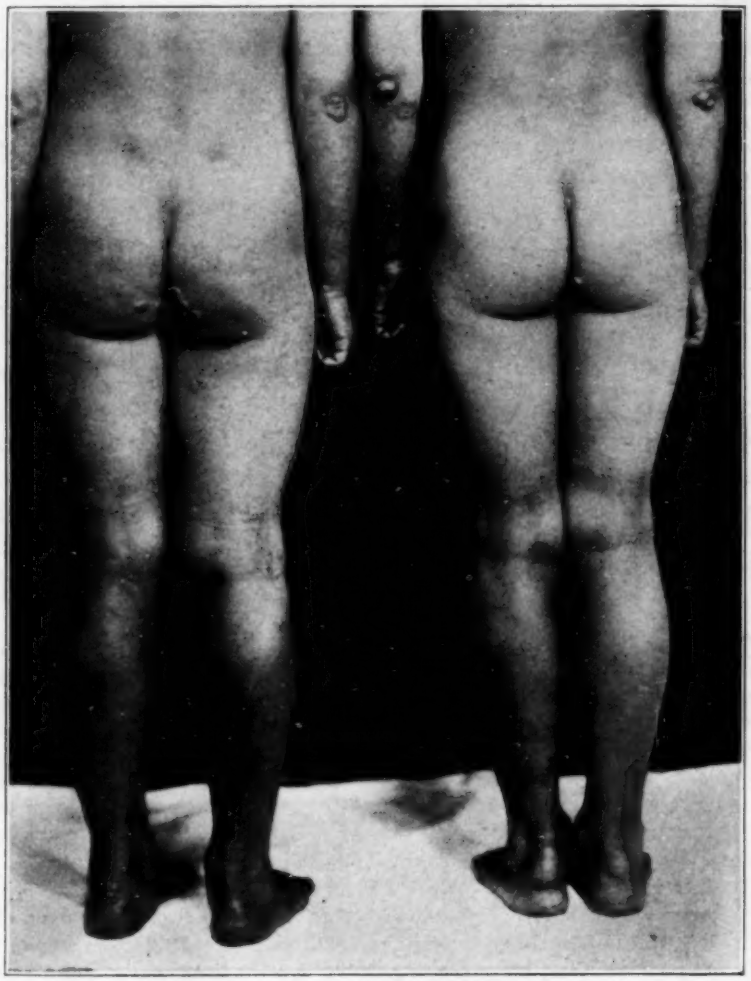
CASE 1.—K. L., a schoolgirl, aged 8 years, was brought to the hospital for advice concerning an eruption of one and one-half years' duration. It first appeared as small pinhead-sized yellowish papules on the elbows. These lesions increased slowly in size, and also appeared over the trunk and lower extremities. At no time did the eruption cause any symptoms. The past and family histories were unimportant. The urine of the parents was negative for sugar and their blood sugar was normal. On examination, the patient was entirely normal except for the cutaneous lesions that were present over the elbows, knees, gluteal cleft, popliteal spaces and achilles' tendon. These lesions varied from the size of a pea to that of an olive; they were the characteristic saffron yellow and had the consistency of xanthomas. It is worthy of note that all the lesions were on the posterior surface of the body, except two small pinhead-sized lesions on the outer side of each knee. The largest lesions occurred over the olecranon and over the buttocks, in which location they reached the size of a pigeon's egg.

CASE 2.—M. L., a schoolgirl, aged 7 years, was the younger sister of a patient whose case was previously recorded. Her eruption was of two years' duration, and the lesions appeared over the elbows six months previous to the onset of the disease in her older sister. The lesions increased slowly in size and number, and on examination revealed a striking similarity of distribution and size to those that occurred in her older sister. In addition, the patient also had a few lesions

19. Pollitzer: J. Cutan. Dis. **28**:633, 1910.
20. Grenaud: Monde méd. **37**:725, 1927.

over the back of the neck, the left forearm and dorsum of the left hand. The color and consistency of the lesions were the same in both cases.

In 1928, Wile, Eckstein and Curtis [21] showed conclusively that the lesions of xanthoma are not primarily due to a hypocholesterolemia and



Xanthoma in sisters.

that the high cholesterol content in the blood in the lipemia of diabetes is merely an associated factor of the disordered fat metabolism.

As noted before, glycosuria was observed in only one group of the familial cases of xanthoma, and hypocholesterolemia is recorded in only

21. Wile, U. J.; Eckstein, H. C., and Curtis, A. C.: Lipid Studies in Xanthoma, Arch. Dermat. & Syph. **19**:35 (Jan.) 1929.

three cases. Case studies on the blood have not been made up to the present when the disease occurred in siblings or in members of the same family. From Wile, Eckstein and Curtis' studies, it would appear that unless the occurrence of the disease in members of the same family was merely accidental, it would have to be due primarily to a familial form of fat metabolism disorder.

The two patients whose cases are reported herein were admitted to the University Hospital, and they were made the subject of a supplementary report by Wile, Eckstein and Curtis, particularly with regard to the nature of the xanthomas, and their results tend conclusively to show that the disease resulted as an apparent familial form of fat disorder due to potential diabetes. Briefly summed up, the studies of these two cases show, as in previously reported cases, that cholesterol existed in the tumors themselves in only about 2 per cent of the total weight of the tumors, and to the extent of 16 per cent of the total lipids present.

In both sisters a marked lipemia was found, circulating fat being present in the blood to the extent of 1,383 and 1,330 mg. per hundred cubic centimeters, respectively. As in previously reported cases, the cholesterol increase in the fat was much less than the increase in other fats.

Dextrose tolerance curves for both children showed a marked decrease below the normal, and prolonged studies established the fact that they apparently belonged in the group of potential diabetic patients.

As in the previously reported studies of these authors, a marked decrease in the number, consistency and size of the lesions could be achieved by a diet low in calories, this caloric decrease and associated tumor involution occurring coincident with a marked decrease in the circulating lipemia.

Herein is recorded an instance of familial xanthoma in sisters occurring with a most extraordinarily symmetric distribution. Chemical studies of the cases suggest that the etiology of familial xanthoma should be looked for in a congenital or hereditary disorder of fat metabolism, in some instances, at least, undoubtedly associated with patients who are potential diabetic subjects.

Abstracts from Current Literature

THE ECZEMA PROBLEM. J. H. STOKES, Am. J. M. Sc. **179**:69 (Jan.) 1930.

Eczema is defined as a dermatitis — a catarrhal cutaneous inflammation aroused by the interaction of two causal groups, the predisposing and the exciting. The former are largely constitutional; the latter are immediate irritant accidents or contacts, their interaction resulting in a cutaneous explosion in one of many forms.

Fourteen predisposing causes are given: race, age, infection, parasites, neoplasms, abnormal blood chemistry, dietary disturbances, unbalanced intake-output ratio, gastro-intestinal disturbances, excessive sexual activity, sensitivity, nervous disturbances, endocrine abnormality and cutaneous dystrophies. Exciting causes are listed as external, allergy-producing, infectious, parasites, trauma and nervous shock.

The mechanism of the production of eczematous lesions by the various agents is discussed in detail, and in conclusion a brief, concise summary of a few cardinal points in the treatment for eczema. A careful search should be made for the external irritant, the carbohydrate intake should be reduced and dermophytosis should be looked for on the fingers, toes and groins. Focal infections should be removed, and gastro-intestinal troubles should be corrected. More reliance should be placed on a complete history, experience and judgment in management, and less on laboratory procedures, sensitization tests and metabolism determinations. Light therapy may be used, quartz light often, roentgen ray sparingly, as well as autohemotherapy and calcium. Dependence on disturbance of the nervous mechanism should be reserved to the last.

JAMIESON, Detroit.

DENDRITIC KERATITIS FOLLOWING THERAPEUTIC INOCULATION OF MALARIA. W. C. FINNOFF, Am. J. Ophth. **12**:978 (Dec.) 1929.

Two cases of painful, well defined, dendritic keratitis with pronounced visual disturbance were presented, one reported to have occurred in the treatment for neurosyphilis. This condition is not uncommon in true malaria and its appearance should be the indication for prompt antimalarial treatment.

HARRY R. FOERSTER, Milwaukee.

GENERALIZED MELANOSIS. STUART C. WAY and S. E. LIGHT, J. A. M. A. **94**:241 (Jan. 25) 1930.

This is the report of a case with observations at necropsy. The primary lesion was probably a pigmented nevus located on the patient's back. This lesion had been present for many years; it was elevated and was subject to constant irritation. The first metastases appeared on the scalp in the form of three or four minute lesions. One month later there was a shower of metastatic lesions involving practically the entire body. They were purplish red and were mistaken for purpura hemorrhagica by many observers. The color slowly changed to black or brown. Many of the lesions finally became nodular. There was involvement of the mucous membranes and conjunctivae, with pigmented strips in the nail beds. There was intense pruritus. The patient was a woman aged 66. There was melanuria. Necropsy showed metastases in the lungs, heart, pleura, peribronchial and retroperitoneal lymph nodes, peritoneum, omentum, suprarenals, bladder, intestine and eye. Histologic examination revealed pigment granules in the tubular epithelium of the kidneys. The article contains some excellent photographs and photomicrographs.

CANCER SUPERVENTION IN SKIN DISEASES. JOSEPH J. ELLER and NELSON P. ANDERSON, J. A. M. A. **94**:382 (Feb. 8) 1930.

The authors point out that the increase in the number of cures of malignant growths is a direct result of the emphasis placed on early recognition of cancer. They go a step further and call attention to the pathologic entities which are sometimes forerunners of cancer of the skin. Included in their list are more than twenty conditions of the skin which are precursors of cancer; syphilis (especially in the mouth); leukoplakia; radiodermatitis; moles; keratoses; kraurosis vulvae; occupational keratodermas, as from tar, pitch and oil; lupus vulgaris; tuberculosis cutis; lupus erythematosus; keratoses due to arsenic; sebaceous cyst; chronic ulcers; Paget's disease of the nipples and extramammary Paget's disease; cicatrices; cutaneous horns; Bowens' disease; papillomas; xeroderma pigmentosum; blastomycosis, and inflammatory dermatoses, such as psoriasis, lichen planus and eczema. The possibility and frequency with which cancer follows these conditions are considered separately and in their approximate order of importance. Factors such as idiosyncrasy and irritation are merely mentioned. The sarcomas and various granulomas, such as mycosis fungoides, are not included in the paper. It is an excellent summary for the practitioner, and it is well suited to the needs of the *Journal of the American Medical Association.*

RATTNER, Chicago.

TRANSPLANTATION STUDIES ON TUMORS ARISING SPONTANEOUSLY IN HETEROZYGOUS INDIVIDUALS. LEONELL C. STRONG, J. Cancer Research **13**:103 (July) 1929.

The tumor cell possesses a specific individuality which is self-regulatory, being transmitted from one cell generation to the next through the process of cell division. The growth of an implant in a given individual is controlled by the activity of certain physiologic host determiners derived from the zygote that gave rise to the individual. Susceptibility and immunity to the implant are definitely inherited according to mendelian principles. Transmission of susceptibility to the growth of the implanted tissue has always followed the laws of mendelian heredity. From these theories the author concludes that the problem of the neoplastic tissue is a problem of genetics and may eventually be solved by genetic methods.

RADIO CHEMICAL REACTIONS. M. C. REINHARD, J. Cancer Research **13**:154 (July) 1929.

The cell, in its simplest form as a unicellular organism, is a complicated mechanism and the effect of irradiation on a dividing cell may not be a direct action on the cell as a whole but on certain constituents or compounds in or about it. Cell life may be a matter of activated molecules and those in a state of higher energy level may be more susceptible to destruction or modification by radiant energy. It is argued that irradiation over a long period, so as to affect a greater number of activated components, should be more effective than massive doses.

THE MALIGNANT CELL. WILLIAM C. MACCARTY, J. Cancer Research **13**:167 (July) 1929.

This investigator, after more than twenty years' study of cancer cells, announces "that it may be stated positively that all malignant cells arise from the regenerative cells of normal tissue." He considers it best to study fresh, unfixed and unstained tissue to recognize the early cancer cell.

THE CARCINOGENIC ACTIVITY OF TAR IN VARIOUS DILUTIONS. W. H. WOGLOM and L. HERLY, J. Cancer Research **13**:367 (Dec.) 1929.

The dilution of tar with glycerin down to 25 per cent neither retards the appearance of malignant tissues nor diminishes the number induced. The mortality is much lower, however, than when whole tar is applied.

SPONTANEOUS MAMMARY CANCER IN MICE. M. C. MARSH, J. Cancer Research **13**:313 (Dec.) 1929.

This investigator of the New York State Institute for the Study of Malignant Disease believes that while the origin of tumors in mice is controlled by heredity, it is affected as well by many environmental factors, some of them little known or commensurable, that tend to obscure the genetic interpretation. Mendelian dominance or recessiveness in heterozygotes is not sharply defined. (These observations are at variance with the arbitrary stand taken by Slye, Strong and others that cancer is a pure problem of genetics.)

HARRY R. FOERSTER, Milwaukee.

THE RÔLE OF THE RETICULO-ENDOTHELIAL SYSTEM IN IMMUNITY: VI. THE EFFECT OF ENDOTHELIAL BLOCKADE ON THE STORAGE AND DISTRIBUTION OF NEOARSPHENAMINE. C. W. JUNGEBLUT and B. R. MCGINN, J. Exper. Med. **51**:5 (Jan.) 1930.

A small quantity of diluted india ink was injected intravenously into guinea-pigs, rabbits and mice, and twenty-four hours later an intravenous injection of a small quantity of neoarsphenamine was made. During the next twenty minutes, the blood of the guinea-pigs showed a marked retention of neoarsphenamine. The rabbits showed a much slower elimination of the arsphenamine from the blood than appeared in the controls. Less arsphenamine was found in the livers of the mice into which injections were made than in the controls.

THE EFFECT OF THE X-RAY ON THE NODULES OF VERRUCA PERUANA. H. R. MULLER and J. R. TYLER, J. Exper. Med. **51**:23 (Jan.) 1930.

Single erythema doses of roentgen ray were found to inhibit the growth of early verruca nodules, and similar doses rendered the skin of monkeys more resistant to inoculation. The results would seem to warrant the use of roentgen rays on verrucous nodules in man.

JAMIESON, Detroit.

NOTE ON THE ETIOLOGY OF PELLAGRA. WILLIAM H. WILSON, Brit. M. J. **1**:101 (Jan. 18) 1930.

Wilson analyzes the statistics of Cluver (*Brit. M. J.* **2**:753 [Oct. 26] 1929) which deal with an outbreak of pellagra in the Durban prison command. The author has established that if the available protein (gross protein less loss in intestine) is reduced to the value of meat protein, by the application of K. Thomas's figures for the biologic value of protein from different sources, diets in which the values so obtained fall below 40 Gm. daily are likely to lead to pellagra in the consumers. With this method, an analysis of the diets used by Cluver indicates clearly that they are of the type that might cause pellagra. The constancy with which the author has been able to demonstrate this deficiency in protein value in the diets of patients suffering from pellagra indicates that the protein deficiency theory of pellagra provides a reasonable explanation of the results.

Wilson points out that the theory of vitamin deficiency of Goldberger was arrived at chiefly as the result of experimental work performed on rats and dogs. He does not accept the usual view that the deficiency disease in rats and dogs is comparable in all respects to pellagra. In rats there are no lesions of the alimen-

tary tract; the dermatitis is not related to exposure to light, and there is a constant hematuria, whereas in man the urinary tract is not affected and the dermatitis is usually excited by exposure to light.

The black tongue of dogs is curable by raw lean beef, whereas later stages are not cured by yeast or yeast extract. Various diets are then analyzed and studied with respect to the rôles played by protein deficiency and vitamin deficiency, and the conclusion is reached that the essential cause of pellagra is a primary or a secondary deficiency in the value of the protein intake relative to the individual requirement, a requirement which may be raised by various conditions. There may be other extrinsic factors, however, and the food deficiency may be only the necessary precursor.

THE DANISH TREATMENT OF ITCH. ALEXANDER CANNON, Brit. M. J. **1**:148 (Jan. 25) 1930.

The "one day cure" has never failed in the author's experience. The following routine is used. After bathing, the entire body, except the head, is anointed. The patient then waits twenty minutes to allow the application to soak in, and then dresses. Twenty-four hours later, the patient again bathes and he is cured. No relapses have been reported in the past seventeen years that the treatment has been used. Itching is relieved in an hour. The formula is complicated and requires care in its preparation. A copy of the formula is incorporated in the article:

"I. 1 kg. of sublimated sulphur is dissolved by heating it gently in 1 kg. of a 50 per cent solution of potassium hydroxide, a clear yellow solution resulting.

II. 225 grams of vaseline and 225 grams of water-free lanoline are mixed with care, no heat being used.

III. To this mixture 375 grams of the solution of sulphur in potash lye (see I) is added.

IV. Fresh zinc hydroxide is prepared by mixing 28 grams of $ZnSO_4$ and 40 grams of a 20 per cent sodium hydroxide. Then this is added to the ointment.

V. Liquid paraffin is added to make a total weight of 1,000 grams.

VI. 5 grams of benzaldehyde is added to check the somewhat disagreeable smell of sulphuretted hydrogen."

RATTNER, Chicago.

THE PHENOMENA OF SHOCK IN URTICARIA. P. VALLERY-RADOT and L. ROUQUES, Ann. de dermat. et syph. **10**:1041 (Oct.) 1929.

The discovery of anaphylaxis threw a new light on the pathogenesis of urticaria. Widal and his collaborators have shown that in most cases of urticaria the outbreak is preceded by definite alteration in the blood and circulatory apparatus. They designated these phenomena as the hemoclastic shock or crisis. Many urticarias show the cardinal features of anaphylaxis; others differ in minor points, while a few appear to be idiosyncratic. The hemoclastic crisis is often difficult to demonstrate; it is latent, but precedes wheal formation.

The authors consider at some length the etiologic factors in urticaria. The relation between urticaria, asthma, migraine and other allergic diseases is intimate. Widal places these disorders in a group characterized by him as the colloidoclastic diathesis.

There are certain adjuvant, as well as direct, factors in colloidoclastic phenomena, such as, disturbances of the autonomic system, endocrinopathies, hepatic hypofunction, infection, reduced alkali reserve and lessened digestive efficiency.

In the treatment for urticaria the authors have found preprandial peptone therapy of value. The underlying principle of this treatment can be utilized in urticaria

due to crystalloids (quinine and other drugs). They also discuss various other well known nonspecific desensitizing methods, such as, autohemotherapy, injections of sodium thiosulphate and calcium chloride.

ACHROMIA PARASITARIA. GOUGEROT, JOYEUX, BURNIER, P. BLUM, J. MEYER and SAÏDMANN, Bull. Soc. franç. de dermat. et syph. **36**:1028 (Nov.) 1929.

This disease has become frequent in France. In these cases *Malassezia furfur* was demonstrated. Experimental study has shown that the depigmentation is due to microbic action. Achromia parasitaria is an atypical form of pityriasis versicolor.

RAYNAUD'S DISEASE: SCLERODACTYLIA. GOUGEROT and J. MEYER, Bull. Soc. franç. de dermat. et syph. **36**:1030 (Nov.) 1929.

The authors record a case of an unusual syndrome, first described by Lortat-Jacob. Their patient had Raynaud's disease, sclerodactylia, myxedematous facies, hypertrophic scars, disseminated telangiectatic plaques and some erythematosquamous and atrophic patches on the soles.

TELANGIECTASIA APPEARING DURING PREGNANCY. GOUGEROT and J. MEYER, Bull. Soc. franç. de dermat. et syph. **36**:1032 (Nov.) 1929.

The patient presented numerous telangiectatic patches only on the uncovered surfaces. The lesions had appeared during the early part of her four pregnancies and disappeared several months after delivery. The condition was familial, two sisters having had similar experiences. The patient had hereditary syphilis, and the authors thought that a syphilitic capillaritis was the probable etiologic factor.

ARSENICAL STOMATITIS. MILIAN and J. FOUQUET, Bull. Soc. franç. de dermat. et syph. **36**:1033 (Nov.) 1929.

While this condition is rare, several incontestable cases have been reported. In the present case of primary syphilis, stomatitis appeared after several injections of neoarsphenamine. Vincent's organisms and streptococci were present. The authors explain the complication as an example of biotropism. In this condition more energetic treatment of the same kind is indicated.

PICRIC ACID DERMATITIS. GOUGEROT and ARNAUDET, Bull. Soc. franç. de dermat. et syph. **36**:1037 (Nov.) 1929.

In this instance, a dermatitis developed after the application of picric acid to a burn of the hand. Percutaneous tests showed sensitization to picric acid and produced a hemoclastic crisis.

TAR EPITHELIOMA. P. BLUM, J. BRALEZ and DE VADDER, Bull. Soc. franç. de dermat. et syph. **36**:1038 (Nov.) 1929.

The patient, a worker in a gas plant, presented an epithelioma of the face which apparently developed on a burn from tar. Several similar cases have been recorded in France.

ANOTHER CASE OF PENILE GANGRENE CURED BY SEROTHERAPY. LORTAT-JACOB, FLANDRIN and POUMEAU-DELILLE, Bull. Soc. franç. de dermat. et syph. **36**:1042 (Nov.) 1929.

The patient presented gangrene following chancroid. He was given polyvalent antigangrene serum (Pasteur Institute) and rapidly recovered.

ZOSTER, VARICELLA, FACIAL PARALYSIS IN A LATENT SYPHILITIC PATIENT. LOUSTE, LÉVY-FRANCKEL and TRIAU, Bull. Soc. franç. de dermat. et syph. **36**:1047 (Nov.) 1929.

The authors report a case of cervical zoster, accompanied by an eruption of the type of varicella, in a latent syphilitic patient. Paralysis of the seventh nerve developed fifteen days after the onset of the zoster. This association is well known since the work of Ramsay Hunt. In this case, the presence of a latent syphilitic meningitis deserved notice.

A SCALP ERUPTION IN FENCERS. E. DELMAS, Bull. Soc. franç. de dermat. et syph. **36**:1056 (Nov.) 1929.

Two cases of a follicular eruption of the scalp are reported. These occurred at points of contact with a mask used by the patients during fencing practice.

TREATMENT OF LUPUS ERYTHEMATOSUS WITH INTRAMUSCULAR INJECTIONS OF A LIPOSOLUBLE GOLD COMPOUND. C. SIMON, Bull. Soc. franç. de dermat. et syph. **36**:1059 (Nov.) 1929.

The author reports the cases of three patients who were treated with a new gold compound. Two of the patients had recurrences after the use of the commonly employed gold compounds or neoarsphenamine. These cases responded slowly but completely to the liposoluble gold salt. The third case showed improvement but not complete disappearance of the disease.

In the discussion, Burnier said that he had not been favorably impressed with his results in the cases of four patients treated with liposoluble gold.

A CASE OF VITILIGO TREATED BY ULTRAVIOLET LIGHT AFTER FRICTIONS WITH OIL OF BERGAMOT. PHIPPS, Bull. Soc. franç. de dermat. et syph. **36**:1065 (Nov.) 1929.

Phipps treated an early condition in a girl, aged 14, by preceding the applications of ultraviolet light with oil of bergamot. The object was to produce increased sensitivity to the ultraviolet rays.

There was repigmentation but it was not maintained. However, when the local treatment was combined with antisyphilitic therapy (because of a suspicion of congenital syphilis) the vitiligo disappeared and had not returned after a year's observation.

THE TREATMENT OF LEPROSY WITH GOLD SALTS. SÉZARY, DÉROT and GUÉDÉS, Bull. Soc. franç. de dermat. et syph. **36**:1071 (Nov.) 1929.

Basing their therapeutic attempt on the apparent relationship of tubercle and leprosy bacilli, the authors employed gold salts in three cases of Hansen's disease. One patient seemed to be temporarily benefited; the other two became worse.

GENERALIZED EPIDERMOPHYTOSIS DUE TO EPIDERMOPHYTON INGUINALE IN A NURSLING. M. PIGNOT and P. PHOTINOS, Bull. Soc. franç. de dermat. et syph. **36**:1075 (Nov.) 1929.

An infant presented irregularly shaped squamous patches chiefly in the diaper region. *Epidermophyton inguinale* was obtained in culture.

ICTERUS OCCURRING DURING ANTISYPHILITIC TREATMENT. LAFOURCADE, J. FOUQUET and NATIVELLE, Bull. Soc. franç. de dermat. et syph. **36**:1080 (Nov.) 1929.

The authors report observations on twenty-three patients. Five cases appeared during treatment with arsphenamine, while eighteen were observed during bismuth or mercury therapy. With the exception of one, or possibly two cases, all were due to syphilis since intensification of the treatment resulted in disappearance of the icterus.

BACILLEMIA DURING AN ACUTE FEBRILE ATTACK IN LEPROSY. A. M. DE CASTRO and L. S. GOMES, Bull. Soc. franç. de dermat. et syph. **36**:1082 (Nov.) 1929.

The existence of bacillemia during the acute stages of leprosy is still in dispute. The authors' observation is a contribution to this question. Their patient developed an acute attack while under treatment. During this attack and for some days afterward, the blood contained numerous Hansen's bacilli.

SULPHUR IODIDE IN THE TREATMENT OF TINEA CAPITIS. H. ALLIOT, Bull. Soc. franç. de dermat. et syph. **36**:1087 (Nov.) 1929.

Alliot used sulphur iodide (10 per cent) in glycerin locally applied with satisfactory results in this disease. Cure was obtained in from one to five months' time.

CUTANEOUS ALLERGY TO EMETIN. LORTAT-JACOB, FLANDRIN and POUMEAU-DELILLE, Bull. Soc. franç. de dermat. et syph. **36**:1088, 1929.

Injections of emetin hydrochloride produced a generalized eruption consisting of numerous erythematous patches. The skin reaction to emetin was negative, but lesions developed after each injection of the drug.

MICHAEL, Houston.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

SIMPLE ROUND ULCERS OF VAGINA. C. F. FLUHMANN, Am. J. Obst. & Gynec. **18**:832 (Dec.) 1929.

The literature contains reports of sixteen cases of ulcus ortundum simplex vaginae. Two additional instances are reported by Fluhmann. The lesion is a chronic nonsyphilitic inflammatory ulcer of the vagina and usually occurs after the age of 40. The etiology is not understood. The differential diagnosis consists in recognizing it from ten other ulcerative conditions that may occur in this situation. Treatment by conservative means is recommended.

EFFECT OF ROENTGEN RAYS ON RETICULO-ENDOTHELIAL SYSTEM. E. A. POHLE, Am. J. Roentgenol. **22**:439 (Nov.) 1929.

The function of the reticulo-endothelial system has been studied by Pohle by recording the elimination of congo red and trypan blue injections in the ear vein of rabbits after exposure to roentgen rays. His results are at variance with those reported by previous investigators. A toxic reaction following injection of trypan blue in rabbits, if preceded by irradiation, is described. This phenomenon has not been reported before. In view of the fact that the reticulo-endothelial system extends throughout the whole organism and as little is known about the factors controlling its function, no theory is offered to explain the results of his experiments but they are simply presented as the basis for further research.

CHANGES IN FINGER NAILS IN PULMONARY TUBERCULOSIS. A. G. HAHN, Am. Rev. Tuberc. **20**:876 (Dec.) 1929.

Pittings or depressions in the finger nails were observed by Hahn in 100 per cent of a group of patients suffering from active pulmonary tuberculosis, as compared with 6 per cent of a group of patients who had been inactive for a relatively short period, and a third group of inactive cases (without symptoms of activity for from one to twenty-five years) in whom this change was found

to be absent in 100 per cent of the cases studied. Therefore, in his opinion the occurrence of these characteristic pittings in a known case of pulmonary tuberculosis should be regarded as indicative of recently active tuberculous disease provided no other disease is present. Hippocratic incurvation was found in 76 per cent of the active tuberculous group, 50 per cent of the inactive tuberculous group and 30 per cent of the ex-patient workers at the sanatorium. This change did not occur in any of the nontuberculous controls (presumably normal). Cyanosis of the finger nails was noted in 66 per cent of the active group as against only 2 per cent of the inactive or chronic group. This change was well marked in all cases in which the disease was rapidly advancing, as evidenced by clinical symptoms and roentgenographic studies. From these observations Hahn believes that cyanosis may be of value in prognosis. Ridging seems to be of less importance than the other changes described.

USE OF GLYCERIN AS TOPICAL APPLICATION IN SUPPURATIVE WOUNDS. M. E. LICHTENSTEIN, Illinois M. J. **56**:425 (Dec.) 1929.

The use of glycerin dressings is not a new procedure, having been employed for a considerable time in various combinations, more commonly in a dilution with an equal part of 70 per cent alcohol. Lichtenstein asserts that glycerin, chemically pure, when applied to a suppurative wound at or slightly above body temperature, aids in diminishing the amount of wound exudate. Spreading lymphangitis and tissue swelling may be inhibited or diminished by frequent applications of this substance. Removal and reapplication of dressings impregnated with glycerin are not painful and do not occasion as much discomfort as dressings commonly do in suppurative wounds. Following the establishment of drainage from an infected wound subsequent to the use of hot wet dressings, glycerin applications are of distinct value in avoiding maceration and the development of superficial infections that commonly follow continuance of hot moist applications.

GRAYING OF THE HAIR. J. A. M. A. **94**:283 (Jan. 25) 1930.

In Queries and Minor Notes recently there was a communication asking whether there is any known remedy for the condition in which gray and white hair becomes gradually yellow and unsightly. A dear old lady with most beautiful white hair said that hers had this tendency but that she kept it in its unusually attractive condition by adding a small amount of ordinary washing bluing to the water with which she rinsed her hair after shampooing it.

INTOLERANCE TO DEXTROSE IN VARIOUS DERMATOSES. A. R. SOMERFORD, Lancet **2**:1140 (Nov. 30) 1929.

Of 120 cases of all types of dermatoses, psoriasis, pruritus, lichen group, eczema, acne and coccogenic sycosis, tested by Somerford only twenty-eight (23.3 per cent) gave normal sugar readings. The other ninety-two showed some deviation from the normal, though in many cases the abnormality was only slight. In most cases it was of the "lag" type, an abnormality which points to some defect in the mechanism by which dextrose is stored in the liver as glycogen.

SIMPLE METHOD OF TREATING CAVERNOUS NEVI. G. B. DOWLING, Lancet **2**:1251 (Dec. 14) 1929.

Dowling has treated five patients by injecting solution of quinine dihydrochloride and urethane; the result has been satisfactory.

EFFECT OF ULTRAVIOLET RADIATION ON INCIDENCE OF TAR CANCER IN MICE. A. C. KOHN-SPEYER, Lancet **2**:1305 (Dec. 21) 1929.

Under the conditions of her experiment, the irradiating of mice with ultraviolet rays as an adjunct to tarring was not found by Kohn-Speyer to produce warts more quickly than tarring alone.

EXPERIMENTAL REPRODUCTION OF LESIONS OF HODGKIN'S DISEASE. C. BRUN, Arch. d. mal. du cœur **22**:666 (Oct.) 1929.

Brun reports that she was able to transmit the characteristic lesions, in one case by three passages from patients to guinea-pigs. Portions of the lymph nodes of two patients who died of the disease were inoculated into the peritoneal cavity of guinea-pigs. In the first case the animal showed loss of weight coincident with hyperleukocytosis and a decrease of red blood cells. It was killed seven months later. In the second experiment the animal died two months after inoculation. In each animal microscopic examination of the lymph nodes showed that they contained the characteristic Sternberg cells. Blood withdrawn from the heart of the first animal was citrated and injected intravenously into two other guinea-pigs. In one animal only 0.5 cc. was injected and it remained healthy. In the second animal 2 cc. of blood was injected; loss of weight, anemia and hyperleukocytosis were noted and it was killed eight months later. Sternberg cells were found in the mesenteric, axillary and inguinal lymph nodes and in the spleen. The suprarenals showed degeneration, but granulomatous transformations were not seen. The subcutaneous inoculation of a piece of liver from this animal into another guinea-pig caused loss of weight and hyperleukocytosis; the animal died ten months after the inoculation, but necropsy could not be done. Another guinea-pig in which pieces of lymph nodes had been inoculated again showed loss of weight and modifications in the blood count and in the cervical lymph nodes Sternberg cells were noted. In all animals bacteriologic examination had not revealed the presence of bacilli; however, the cultivation of a piece of a mesenteric lymph node from the guinea-pig in which the original lesions had been reproduced showed, after three weeks, colonies similar to those of tubercle bacilli. Brun states that in guinea-pigs the evolution of the disease appears to be as slow as in man in "chronic" types of cases, but that on the whole the evolution is variable and, as seen in one guinea-pig, a latent period may occur.

MILK AND DIET FOR TREATMENT OF ECZEMA IN INFANTS. L. RIBADEAU-DUMAS, R. MATHIEU and WILLEMIN-CLOG, Paris méd. **2**:491 (Dec. 7) 1929.

Ribadeau-Dumas et al. direct attention to the importance of an analysis of the milk used in feeding infants affected with eczema. Examinations have shown that hyperproteinemia is always an associated condition with disorders of water metabolism. Treatment should therefore be directed not only to better local functioning of the tissues but also to the relief of disorders of metabolism. It was furthermore noted that breast-fed infants more often had eczema than those fed artificially. The authors state that this may be due to overfeeding or improper balance of foods causing gastro-intestinal disorders. Dyspepsia caused by excess of butter and casein in the milk has frequently been reported by various authors. Control of the mother's diet may be helpful, although, once established, eczema does not yield to dietary regulation alone.

NEURODERMATITIS. R. SABOURAUD, Presse méd. **37**:1541 (Nov. 27) 1929.

Sabouraud discusses the etiology, localization and treatment of neurodermatitis. He considers the old terminology "circumscribed lichen" more appropriate, as it characterizes the lesion without pointing to its origin. Although this condition frequently occurs in subjects with mental depression, Sabouraud states that he invariably found *Streptococcus impetiginis* in cultures of the fluid obtained after scarification of the lesions. Of significance is the fact, according to Sabouraud, that the treatment is identical with that used in chronic impetigo of the scalp, namely, daily applications of iodized alcohol, the use of a coal tar ointment, fresh air and ultraviolet irradiation. Roentgen rays are not advised as they cause loss of hair. The duration of treatment is at least three months.

NERVOUS COMPLICATIONS OF CHICKENPOX. F. FASELLA, Policlinico (sez. med.) **36**:566 (Nov. 1) 1929.

Fasella reports a case of polyneuritis developing after chickenpox. A boy, aged 6, with a negative personal and family history, six days after the onset of a moderate eruption of chickenpox, when the disease had practically subsided and the fever had ceased, was seized with fever and severe pains in the lower limbs. A complete paralysis of the lower limbs developed. There was a disappearance of the patellar and achilles reflexes, and severe pain in the nerve trunks of the sciatic and femoral nerves. The symptoms disappeared to a certain extent after two days, but the same manifestations developed in the upper limbs. The manifestations subsided rapidly, and, at the end of a week, had disappeared without leaving any traces. The author attributed the symptoms to the action of the chickenpox virus.

PROPHYLAXIS OF LEPROSY IN EARLY CHILDHOOD. L. E. PIERINI, Semana méd. **36**:988 (Oct. 3) 1929.

Pierini says that asylums for children of lepers are necessary in Argentina. He states that 42 per cent of the children of lepers who continued living at home acquired the disease in from three to six years. Clinically suspected lesions became positive within five months of their appearance. Only 0.5 per cent of the children of lepers who were separated from their parents developed the disease. The youngest patient seen by the author was 4 years of age.

SYPHILIS D'EMBLÉE. M. TIÈCHE, Schweiz. med. Wchnschr. **59**:1097 (Nov. 2) 1929.

Tièche asserts that there are two forms of syphilis d'emblée, a hematogenous and a lymphogenous. The hematogenous type develops after blood transfusions if the donor has syphilis. The lymphogenous type becomes manifest in inflammations of the inguinal lymph nodes. The author gives a detailed description of two cases of the lymphogenous form. Although syphilis d'emblée is characterized by the absence of a primary lesion, the author thinks that a small, perhaps microscopic, initial sore exists, but that it is not noticed. He stresses that patients with inflammations of the inguinal lymph nodes should be kept under careful observation for several weeks, even if other symptoms of syphilis are not present. If the serologic test at first gives negative results, it should be repeated from time to time. In order to prevent the hematogenous form of syphilis d'emblée, the author states that persons who have had syphilis should never act as blood donors. A negative Wassermann reaction is not always sufficient proof for the absence of syphilis. Persons supplying blood should be requested to sign a statement that they have never had syphilis.

TROPHIC POSTENCEPHALITIC ULCERATIONS OF NOSE AND OF CHEEK. E. SCHLITTLER, Schweiz. med. Wchnschr. **59**:1121 (Nov. 9) 1929.

Schlittler reports the case of a boy, aged 14. Three years previously he had shown during several weeks increasing languor and drowsiness. After that he was less active than before and appeared apathic and dull and weak. Later he developed coryza and scratched his nose continually. A rapidly growing ulceration developed. The patient's general condition became steadily worse. The application of ointments brought temporary improvement but the ulcer did not heal entirely. The right ala nasi was almost entirely destroyed, and the ulcer extended down to the angle of the mouth. Moist bandages had a cleansing effect on the ulceration, but the patient scratched the sore continually; when he was prevented from doing so he became restless. Serologic tests for syphilis gave negative results, and antisyphilitic treatment of the ulcer was of no avail. The ulceration

increased steadily. The results of clinical, bacteriologic and microscopic examinations indicated that trophic, postencephalitic disturbances were the cause of the ulceration. The fact that the patient showed hypersalivation and typical manifestations of parkinsonism confirms this diagnosis. Several months later the ulceration started to heal.

CHEMICAL RESEARCHES ON SKIN TISSUES IN EXPERIMENTAL ROENTGEN INTOXICATION. E. URBACH and H. SCHNITZLER, Klin. Wchnschr. **8**:2179 (Nov. 19) 1929.

Urbach and Schnitzler investigated the pathogenesis of roentgen intoxication in experiments on animals. Chemical tests of the blood and of the skin tissues proved that this condition was a protein injury. It could be demonstrated that after intensive roentgen irradiation the total nitrogen and especially the residual nitrogen were increased. The increase in the total nitrogen content of the blood was about 10 per cent, whereas in the skin tissues it ranged from 20 to 30 per cent. The residual nitrogen was increased up to 300 per cent. That the poisoning is generalized is proved by the fact that the chemical changes in the tissues that have not been exposed are the same as in the irradiated tissues. It was found also that although the nitrogen content was increased, the chlorine content was reduced. This disproves the theories of other authors who assumed that in roentgen intoxication the tissues retain sodium chloride. Urbach and Schnitzler maintain that the disintegration of protein is the main factor in this form of poisoning and it may be recognized by the increased quantities of nitrogen, especially of residual nitrogen. They assume that as favorable results were attained with sodium chloride, this substance provides a certain protection for the protein.

PATHOGENESIS AND TREATMENT OF ENDOCRINE DERMATOSES IN WOMEN. M. SAMUEL and L. STRAUSS, Med. Klin. **25**:1698 (Nov. 1) 1929.

Samuel and Strauss report their observations on 290 women with various forms of dermatoses. The majority of the patients had some form of pruritus. Pruritus vulvae with or without disturbances of the vaginal secretion, generalized pruritus with itching over the whole body, intertrigo of the vulva and anal eczema were the conditions most commonly observed. The authors state that the majority of these women were in the menopause, and among the younger patients married women were comparatively more numerous than unmarried ones. Concerning the etiology of these dermatoses, the authors state that in the majority of the patients the sugar content of the blood was markedly increased. In other instances the dermatoses could be traced to functional disturbances of the ovaries or to dysmenorrhea. In discussing the treatment, the authors state that many cases were refractory to the usual therapeutic methods such as baths and the application of ointments and powders. Because the blood sugar content was increased in many patients, insulin injections were tried. For several days the women received from 10 to 15 units of insulin, and the carbohydrate content of the diet was reduced. As a result of this treatment the pruritus and the hyperglycemia disappeared. In some instances in which the dermatoses were caused by ovarian or menstrual disturbances, the insulin injections were likewise helpful.

ECZEMA CAUSED BY BAKELITE VARNISH. F. BLUMENTHAL and K. JAFFÉ, Med. Klin. **25**:1848 (Nov. 29) 1929.

Blumenthal and Jaffé describe seven persons who had weeping eczema on the uncovered portions of the body, especially the hands. All of these patients were employed in an industrial plant, where they worked with bakelite varnish, oil of turpentine, shellac, wood oil, benzene and hard paper. When the patients remained away from work and were treated properly, the eczema healed. In order to determine which of the various substances that the patients had worked with had

caused the eczema, the authors made skin tests. It was found that the bakelite varnish was the cause of the eczema. The authors further investigated which of the various constituents of bakelite varnish caused the eczema. They found that all who had developed eczema showed a hypersensitivity to phenol.

NEW SYMPTOM OF GERMAN MEASLES. K. STOLTE, Monatschr. f. Kinderh. **45**:206 (Nov.) 1929.

Stolte believes that in German measles profuse sweating on the penultimate but not the ultimate night before the appearance of the exanthem is of much more frequent occurrence than is generally supposed. The fact that on the following day and night the child feels perfectly well has caused the diagnostic value of this symptom to be underestimated.

ULTRAVIOLET IRRADIATION IN ERYSIPELAS IN NURSLINGS. J. BECKER, Strahlentherapie **34**:205 (Oct. 23) 1929.

Becker calls attention to the fact that the mortality in erysipelas is inversely proportional to the age of the patient and heretofore has been extremely high in nurslings. In eight infants (aged 18 days, 20 days, 3 weeks, 6 weeks, 10 weeks, 6½ months, 9 months and 12 months) with erysipelas treated by means of ultraviolet irradiation with one and one-half times the individual erythema dose only one death occurred and that was in an infant (aged 20 days) in whom erysipelas developed following an operation for umbilical hernia and who died from septic thrombosis, peritonitis and bronchopneumonia. In some of the patients who recovered, the erysipelas was of the most malignant form.

COMBINED LOCAL AND UNIVERSAL LIGHT TREATMENT IN TUBERCULOSIS OF SKIN. A. REYN, Strahlentherapie **34**:13 (Oct. 23) 1929.

Reyn states that at the Finsen Institute in Copenhagen all forms of tuberculosis of the skin are now treated by combined local and universal irradiation. Less time is required, the results are better and recurrences are rarer with this form of treatment than with local light treatment alone.

UNUSUAL CASE OF CEREBRAL SYPHILIS IN A GIRL AGED NINE. G. PAPP, Wien. klin. Wchnschr. **42**:1503 (Nov. 21) 1929.

Papp reports the case of a girl, aged 9, who suffered from hemiplegia and aphasia. The child had been apparently healthy until the day before she was brought to the hospital. Then she had complained of feeling weak and tired. After she had slept for several hours, she could not speak any more, and she also showed signs of a beginning paralysis. Because the symptoms became more severe, the child was sent to a hospital. The author gives a detailed report of the results of the examination. He states that the Wassermann reaction of the blood and of the cerebrospinal fluid was strongly positive. Under the influence of antisyphilitic treatment the paralysis gradually decreased. Because the patient contracted diphtheria, the antisyphilitic cure was interrupted but later it was resumed. However, the Wassermann reaction remained positive. It could not be definitely determined whether this was a case of congenital or of acquired syphilis. Most of the characteristic signs of congenital syphilis were absent, and the mentality of the girl was normal. After the birth of the child such symptoms as vesicles, sores and eczema had not been noticed. The mother had had no abortions and another child, who was three years older than the patient, was entirely healthy. This child as well as the father gave negative Wassermann reactions, whereas the reaction in the mother was strongly positive. The author thinks that by means of a prolonged treatment it might be possible to counteract the syphilis. However, he questions whether the spastic hemiplegia will ever completely disappear.

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

Special Meeting for Professor Jadassohn, June 21, 1929

H. R. Foerster, M.D., *President, Presiding*

Tuberculosis Resembling Chancre. Presented by Dr. Ormsby.

A young woman, aged 13, was presented to illustrate an uncommon type of cutaneous tuberculous. The primary lesion occurred near the inner canthus on the left side, and was first seen as an ulcer on Jan. 27, 1929, at which time it had been present for seven weeks. Coexistent with this was a marked glandular involvement of the submaxillary glands on the same side. Clinically, the disorder resembled syphilis, so a Wassermann examination was made. A careful search for spirochetes was also made, with negative results. This search continued over a period of two weeks. At the end of four weeks' observation, the crust fell spontaneously, and typical brownish lupus nodules were evident. Roentgenotherapy with general treatment directed toward the relief of the tuberculosis was employed successfully.

The past history of the patient revealed suggestions of tuberculosis. She had been under observation since the age of 2, for the treatment of eczema and other cutaneous diseases. Two roentgenograms were made of the lungs preceding the occurrence of this lesion, neither of which showed definite tuberculosis, but both were suggestive.

At present there remained only a scar at the site of the primary lesion, and the relics of the glandular involvement.

DISCUSSION

Professor Jadassohn: This case was especially interesting to me. I know well the publication by Bruusgaard, who published his case, before we knew anything about the primary complex of the skin. Since his publication, there has appeared another publication of this type of tuberculosis which also is very interesting, because in the beginning there was a primary tuberculous ulcer on the foot and on the glands in the inguinal region. Without any treatment this became better, but the primary ulcer turned into a tuberculous lupus, and because of this we can conclude it to be a case wherein the skin was not allergic in the beginning of the infection. Therefore, at first a primary ulcer developed, and then the skin became allergic and the primary lesion turned into real lupus vulgaris. In the present case no evidence of lupus is to be seen in the cured primary lesion.

These cases are of great importance for our knowledge of the development of tuberculosis in the skin. It would be interesting to examine them as early as possible with tuberculin. It might be found that in the beginning the skin does not react (normal, nonspecific allergy). When the allergy develops later, this may lead either to a cure or to the development of some other form of tuberculosis, such as lupus.

Dr. Sulzberger: Last year Dr. Ormsby showed this case to Professor Bloch and me. I think that it must have developed much in the same manner as the primary lesion on the foot which Professor Jadassohn has just mentioned, for at the time we saw the case, Professor Bloch made a diagnosis of lupus. The lesion then presented the picture of a typical small lupus vulgaris with a few apple jelly nodules.

Dr. Ormsby: The only point that I think will have to be proved in the future about these cases is whether they are examples of inoculation tuberculosis or

whether the infection is endogenous, locating in the skin and in the glands at the same time. Clinically, the early lesion is these cases, with its attendant glandular enlargement in the vicinity, very closely resembles extragenital chancre. This case was so considered for some time until syphilis was definitely excluded by repeated negative observations in the dark field and negative Wassermann reactions. The primary lesion here healed, and the regional adenopathy disappeared under roentgenotherapy, together with a tuberculosis regimen as to diet and outdoor life.

LUPUS ERYTHEMATODES. Presented by DR. ORMSBY.

A male patient, aged 33, had a disorder of from five to ten years' duration. The history and description of the lesions were recorded in the transactions of the May meeting of this society.

The lesions were situated on the forehead and ranged from the dime-sized to small, palm-sized, circinate patches with pink, smooth, atrophic centers and slightly elevated reddish-brown margins. Under diascopic pressure, brown nodules remained in the margins. No subjective symptoms were present.

DISCUSSION

PROF. JADASSOHN: I believe this was a case of sarcoid of Boeck of the circinary type. One cannot make an absolutely certain diagnosis of this disease without a histologic examination. Cases of sarcoid of the circinate form are not frequent in our material, and they are interesting from the standpoint of allergy. In those lesions that have spontaneously healed in the center, it would be interesting to make local tuberculin tests to differentiate the cured center, the border and the skin around the lesion.

DR. ZWICK: May I inquire the result of the Wassermann test? The cutaneous allergic phenomena of syphilis simulate those of tuberculosis so closely at times, that in the present case I would hesitate to rule out a syphilid at first sight.

DR. ORMSBY: When we first saw this patient we considered syphilis, some form of tuberculosis such as sarcoid or lupus erythematodes (Leloir) and lepra. We have seen a circinate leprous lesion that resembled this very closely, but we ruled out all except tuberculous lesions. We did not place it definitely, but favored a diagnosis of lupus erythematodes (Leloir), which is really tuberculosis with active, small, apple jelly brown nodules in the margin. I think we cannot say at this time positively whether it is lupus erythematodes (Leloir) or miliary sarcoid.

LUPUS MILIARIS DISSEMINATUS FASCIAE (ACNITIS). Presented by DR. ORMSBY.

A male patient, aged 33, had a disorder of four months' duration. The lesions were situated on the face and neck and behind the ears. Lesions were noted first on the forehead, later beneath the eyes and subsequently on the areas noted. There had been no subjective symptoms. Treatment for syphilis had been without effect.

On examination the lesions were found to be situated on the forehead, lower lids, the sides of the nose, the contiguous portions of the cheeks, on the chin and neck and behind the ears. They were match-head to lentil sized, bright to brownish-red, solid papules and nodules, a number of which were capped with pustules. On applying diascopic pressure, a brown discoloration remained. On certain areas the lesions were group-forming patches.

DISCUSSION

PROF. JADASSOHN: When I saw this patient I told Dr. Sulzberger that this was one of the cases of lupus miliaris with a transition to acnitis. In such a case I think it is not possible to say with certainty whether it should be called lupus miliaris or acnitis. There is even a third form, a small nodular sarcoid. The three forms resemble each other so closely that, while we have cases which are

surely only miliary lupus, others which are surely only acnitis, and still others in which we can make the certain diagnosis of nodular sarcoid of Boeck, there are, nevertheless, some cases in which the three diseases cannot be differentiated. It is not unusual to see infiltrated nodules in lupus miliaris. In one case I made a diagnosis of acnitis, but when Boeck came to Bern and I asked him what the condition was, he said it was his sarcoid. Lupus miliaris is one of the anergetic forms and usually a reaction to tuberculin is not obtained, or only to large doses. In all these forms the histologic lesions are extremely circumscribed. The difference between lupus miliaris and the sarcoid of Boeck is the pronounced tendency of the former to central necrosis, which can sometimes be seen even macroscopically and which does not exist or rarely occurs in the sarcoid. I am quite convinced that Dr. Ormsby's diagnosis is the same as we would make in Breslau.

DR. SENEAR: I am interested in Professor Jadassohn's remarks about this case, because, when the patient appeared, he resembled a patient who was shown by the late Dr. Quinn, and also one whom I showed several years ago with definite apple jelly lesions, which later became pustular and still later necrotic in the center. Several biopsies were made in that case and just what Professor Jadassohn has described was found—some specific tuberculous nodules and some of less specific character.

DR. ORMSBY: I am very much pleased to have Professor Jadassohn's opinion and to find that he views the case in the same way that we do. We have so little tuberculosis of the skin in this country that we are handicapped, and the classification is very difficult for us.

HYPERPIGMENTATION, HYPERTRICHOSIS, AND MORPHEA. Presented by DR. ORMSBY.

A girl, aged 12, had a disorder of six and one-half years' duration. When first seen, at the age of 7, there was a band of hyperpigmentation around the neck, and the pigment extended over the back, covering most of this area, and over the sides of the trunk, involving the chest almost to the center. The abdomen to the groin was also hyperpigmented. At that time there was a superficial band of morphea, 12 by 4 cm., situated over the epigastrium to the left of the median line. In addition, there was marked hypertrichosis on the nucha and forearms. The general health of the patient was normal and she was of normal size for her age (ARCH. DERMAT. & SYPH. **11**:845 [Nov.] 1924).

At the time of presentation the hypertrichosis was more reduced. The pigment increase was reduced so much that it was hardly more than that seen in normal persons. The old patch of morphea had cleared up, but a new one had recently developed on the upper portion of the back. This lesion was perfectly white and about the size of a silver half dollar. The patient was well and weighed 122 pounds (55.3 Kg.). Menstruation was established one year before presentation and was normal. The basal metabolic rate was +5.

During the early years of her observation, the treatment employed consisted chiefly of the administration of thyroid extract in small doses. A decided improvement had occurred since the first observation of the case.

DISCUSSION

PROFESSOR JADASSOHN: This case is interesting, because, as Dr. Ormsby states, there seems to be not a coincidence but a relationship between the scleroderma, the pigmentation and the phthisis. It is exceptional in my material to find morphea proved to be combined with a general endocrine disturbance. I believe, after looking over the literature, that morphea is more frequent in the United States than in Breslau. In this case, it is natural that one finds such combinations more frequently. It is also interesting that this case shows the small intrafollicular keratoses which are to be found sometimes over the whole spot of the scleroderma and sometimes only on the border. I have seen this in many cases, and it has always been very pronounced.

ACUTE HYPERTRICHOSIS. Presented by DR. ORMSBY.

A woman, aged 57, had a disorder of seven weeks' duration. She stated that the new growth of hair occurred practically over night and increased rapidly during the time designated. The basal metabolism was +20. There were no other disturbances or abnormalities.

On examination it was seen that there was a marked new growth of hair on the entire face and neck. The new hairs occupied not only the cheeks in the usual location, but occurred on the nose and forehead. The hair was chiefly of the lanugo type.

DISCUSSION

PROFESSOR JADASSOHN: I never saw a case like this one. It is quite extraordinary, and I do not recall having seen such a condition described in the literature.

DR. ZWICK: I should like to know whether Dr. Ormsby sees a relation between the basal metabolism and the hypertrichosis. Does he see this relationship so often that he feels justified in attributing the condition to such a connection?

DR. ORMSBY: This is the first time that I have ever seen a patient of this type, but I have seen some extraordinary cases of hypertrichosis develop in connection with pregnancy, and have seen some remarkable things develop and disappear at the menopause. Functional and organic disorders of the thyroid at times have a marked effect on the growth and nutrition of the hair. I have seen the hair fall extensively in thyroid disturbance. On account of the fact that this woman has such a high basal metabolic rate I feel justified in using therapy to correct that condition. We shall use both roentgenotherapy on the thyroid and compound solution of iodine internally. So far as I know, the hypertrichosis in this patient is unique.

BLASTOMYCOSIS. Presented by DR. SENEAR.

M. L., a man, aged 71, who was shown at the May meeting of the society, noted a swelling with the formation of groups of hard nodules in the right submaxillary region two years prior to presentation. Since then, the swelling and induration had progressed, until it involved the entire right side of the face in a mass of woody induration, with extension under the chin to involve the left cheek to a lesser degree. Ulceration of a puckered, involuting character was noted in the left parotid region. A few isolated lesions were also noted on the neck and upper part of the chest, and the middle portion of the tongue was the site of a well defined woody induration.

Cultures from various areas had shown only *Sarcinae* and *Staphylococcus aureus*. No fungi had been found, except some noted in the first smears examined from the lesions, which showed yeasts that gave the suggestion of endosporulosis. No budding was seen. There had been marked resolution of the induration and swelling under potassium iodide therapy.

BLASTOMYCOSIS. Presented by DR. FINNERUD.

A well nourished man, aged 32, had a cutaneous eruption of general distribution of more than two years' duration. It was first noted as a wartlike lesion on the right wrist, and soon thereafter appeared on the face and elsewhere. He had been under observation at the Cook County Hospital on several occasions, in the service of Dr. Oliver and Dr. Finnerud, and at one time had twenty-eight active lesions. He had responded well to the combined potassium iodide, neoarsphenamine and roentgen therapy.

At the time of this presentation, there were three active, coin-sized, characteristic lesions of the face. Budding yeasts of *Blastomyces* type were demonstrated in a potassium hydroxide preparation.

BLASTOMYCOSIS. Presented by DR. OLIVER.

A Mexican woman, aged 38, had a condition that existed for the past three years. The eruption first appeared on the feet with severe itching, followed by

swelling, then by the development of papulopustules. Then the condition appeared on the left side of the face, then on the forearms, the body and the hip. The lesions were quite painful when irritated.

Two months after the onset she consulted a physician, who gave her some intravenous therapy for two years, without improvement.

The essential observations were telangiectatic, red lesion, resembling a burn, surrounded by an irregular, crusted, indurated, raised border on the face, and lesions on the arms, consisting of sharply demarcated, punched-out ulcerations, with undermined borders, on a fiery red base, from which a discharge exuded.

BLASTOMYCOSIS. Presented by DR. HEDGE.

A farmer, white, aged 68, first noted a granulating mass on the right wrist thirteen years before presentation. Smears from the pus and the biopsy revealed *Blastomyces*. The first lesion was a small papule which increased in size gradually, in spite of the use of iodides internally, and iodine and copper sulphate at different times locally. The Wassermann reaction was negative. No evidence of systemic complications was discovered. Roentgen and ultraviolet ray therapy had had little effect.

Dr. Hedge felt that the area was too large for the successful use of carbon dioxide snow, and advised that the lesion be curetted away, to be followed by the use of iodine dressings, and as soon as a thin crust was formed, by applications of a very concentrated form of iodine.

DISCUSSION

PROFESSOR JADASSOHN: I am thankful to have had the opportunity of seeing these cases. It was interesting to see them and to compare them, especially the systemic cases.

Perhaps it would interest you to hear that when I saw the first case in the group, with the fine, papillomatous border, and when I saw a similar case in Philadelphia, I thought the condition must be a certain form of tuberculosis which is not well known even in Europe, or at least in Germany. I refer to a form of tuberculosis showing central involution and a very narrow border that is very finely papillomatous, and has so little keratosis that one cannot make a diagnosis of tuberculosis verrucosa, although this condition belongs to the same group.

Such a form of tuberculosis can also develop out of circinary sarcoids, especially when the skin becomes allergic.

DR. MICHELSON: I have seen quite a number of cases of actinomycosis, and we try to classify the cases as to type under three forms: (1) the purely cutaneous type; (2) the type beginning in the skin and involving the deeper parts; (3) the type that begins in the deeper parts and then involves the skin.

I also want to say that the prognosis in actinomycosis should always be guarded, as it is a very serious disease.

DR. ORMSBY: We feel that Chicago is the home of blastomycosis, because much of the pioneer work in the disease was done here. In its early history, many of our European colleagues doubted its entity, considering our cases as tuberculosis, syphilis or carcinoma contaminated with secondary yeast infection. At the International Dermatological Congress held in 1907, I demonstrated specimens of inoculated animals, showing the disease in various organs together with cultures of the organism and histologic sections taken from patients, which were accepted.

The first systemic case was recorded by Buschke, the second by Gilcrist and Stokes, and the third was recorded here in Chicago. The last was completely worked out, showing lesions and organisms in practically all of the tissues and organs of the body.

The cutaneous lesions in the purely cutaneous cases are of a classic type, and can be clearly differentiated clinically from all other diseases, while the cutaneous lesions of systemic cases resemble several other conditions and are not in themselves pathognomonic.

Blastomycosis is apparently much less prevalent now than it was twenty-five years ago.

DR. OLIVER: We have one case of systemic blastomycosis in addition to that of the woman who was shown today. The patient is a young man with four or five skin lesions. He was in the Municipal Tuberculosis Sanitarium for several weeks, and was discharged because the tubercle bacillus was not found. After heavy doses of neoarsphenamine and sodium iodide intravenously, the disorder is clearing up, which does not occur in many of the systemic cases.

DR. LIEBERTHAL: It was interesting to hear Dr. Ormsby's remarks. Soon after the publication of the case of Drs. Hyde, Bevan and Hektoen, one was presented before the Chicago Medical Society in 1899. I was asked to discuss the latter. I suggested that in these cases we might have to deal with tuberculosis or carcinoma on which *Blastomyces* had been secondarily implanted, as the clinical and microscopic signs looked similar to those. Later observations, however, proved conclusively that this opinion was erroneous.

DR. SENEAR: When I first saw the case that I presented I felt as did Dr. Michelson, that we were dealing with a secondary lesion. We are still openminded. There is dense infiltration of the tongue, and the infiltration in the axillary glands and elsewhere does not coincide with our conception of blastomycosis, but the improvement has been so marked under treatment with potassium iodide that we have felt that the condition was due to a mycotic infection.

DR. FINNERUD: The second case in this group has responded very well to therapy, and only three lesions are showing any activity at present. The patient has been shown a dozen times or more in the clinic, and each time the characteristic organisms have been demonstrated. Two or three years ago, one of the men at the Cook County Hospital reported a case involving the conjunctiva and was able to find only three other cases on record. Since that time we have had three other cases involving the conjunctiva.

COCCIDIOIDAL GRANULOMA. Presented by DR. ZEISLER.

An aviator, aged 36, was admitted to the Cook County Hospital with a condition diagnosed as blastomycosis. One year previously, following a hunting trip in the San Joaquin Valley, he noted a "pustule" on the side of his nose. This lesion disappeared under treatment with radium, but was followed two and a half months later by similar lesions on the forearms, the body and other regions. He had received treatment with iodides, arsphenamine and the roentgen ray on the assumption that the disorder was blastomycosis. Three Wassermann tests had been negative. The greatest benefit was derived from large doses of iodides and roentgen ray.

The eruption consisted of exclusive vegetating fungoid masses around the upper eyelids, ears, nostrils and cheeks. There were also many apparently healed, atrophic lesions on the trunk and on the upper extremities and a few crusted papules in which the disease was still active. Cultures and smears for the *Coccidioides immitis* type of organism were positive. Before the pathologic report was made the diagnosis of mycosis fungoides was entertained. (Cultures were demonstrated.)

DISCUSSION

PROFESSOR JADASSOHN: I believe that this disease, as well as blastomycosis, is especially interesting to us because the same questions we have studied in tuberculosis, syphilis and leprosy also arise here. The skin lesions point to the importance of local allergic phenomena in their development.

The influence of the internal disease on the course of the skin lesions recalls analogous observations, especially in tuberculosis.

DR. ORMSBY: Years ago when blastomycosis was considered to be purely a local disorder, I did some work with Howard Morrow comparing coccidioidal granuloma that occurs in California and blastomycosis as we see it here. We

exchanged cultures, and the cultures that came from California grew here and ours grew there. Notwithstanding these facts, the major portion of cases of coccidioidal granuloma have originated in a particular section of California and practically no cases have occurred elsewhere. On the other hand, blastomycosis is rather widespread over this country but rare in California.

DR. ZEISLER: Professor Jadassohn is not the only one who does not recognize this disease. We did not recognize it in this case, and the pathologist made the diagnosis for us. We do not see enough cases of coccidioidal granuloma here to recognize it readily. This case is extraordinary on account of the multiplicity of the skin lesions, and because it presents many points of difference from the cases of blastomycosis seen in Chicago. Lesions of the lower eyelid are often found in blastomycosis, but in this case, the lesions attack the upper eyelid. We see scarring but not of the same type. This case is apparently purely a cutaneous infection with *Coccidioides immitis*. The lungs and bones are not involved. We hope that by the use of antimony and potassium tartrate, which has brought about a cure in some cases, and by the use of iodides we may be able to cure the patient.

DR. LINDSAY, Pasadena (by invitation): We have quite a number of cases of this type in Los Angeles now, and almost every physician who gets such a case turns it over to Dr. Jacobson who has studied the disorder quite intensively for several years. He has found that the condition can be improved in many of these cases by administering intramuscular injections of colloidal copper.

We see a good many cases of blastomycosis, the condition usually being imported from Chicago, and the coccidioidal cases seem to be becoming more prevalent. Nearly all of these patients come from the San Joaquin Valley. The condition is caused by an endogenous spore in the tissues, but if we plant a culture on culture medium, a mycelium grows. Some of Dr. Jacobson's patients have been apparently cured, but they were Mexicans, of whom it is always hard to keep track. Nearly all of them die. I think I would not have been able to recognize Dr. Zeisler's case from the skin lesions alone. Most of the ones I have seen in Los Angeles look more like blastomycosis cases of the systemic type.

ACRODERMATITIS CHRONICA ATROPHICANS, GENERALIZED LICHEN PLANUS OR POIKILODERMA? Presented by DR. ORMSBY.

A woman, aged 50, had a disorder which was of thirty-seven years' duration. (For the history and description of the lesions, see ARCH. DERMAT. & SYPH. **18**: 304 [Jan.] 1928; **20**:388 [Sept.] 1929.)

Since being shown at the annual meeting in January, 1929, the patient had been under continuous treatment with thyroid, and marked improvement occurred. Most of the thickened areas had disappeared, together with the lichenoid or papule-like areas that were generally distributed. Even the telangiectasia seemed to have been lessened. The local treatment was unimportant, and the improvement apparently could be attributed to the thyroid extract.

DISCUSSION

PROFESSOR JADASSOHN: Of course I cannot make a diagnosis in this extremely interesting case. The fact that there were papules and scaling, and that these disappeared on treatment with thyroid recalls a case published by Tryb. In this case the skin lesions developed in a relatively acute manner after an infectious disease.

We compared Tryb's histologic slides with those of my first case of myxedema circumscriptum tuberosum, published by Doessekker. In both cases there was a similar deposit of mucin, but in Tryb's case there was more acute inflammation, while the slight inflammation in my case seemed to be explicable by the reaction to mucin as a foreign body. One must also consider the relationship of these cases to poikiloderma and to calcification of the skin. A case published in Breslau as poikiloderma showed infiltration with mucin and later, calcification.

The latter exists also in sclerodermatoid cases. In its present state, Dr. Ormsby's case recalls disseminate essential telangiectasia, first described by Osler. It is interesting that this disease is doubtlessly related to changes in the genital organs in women, for it may develop during pregnancy and disappear after delivery.

DR. ORMSBY: I am very appreciative of the opinion of Professor Jadassohn. This case has puzzled us greatly. We thought of poikiloderma and of lichen planus, and the extraordinary thing is that within the last six months there has been such a marked change under endocrine therapy. We shall prosecute the treatment along the lines Professor Jadassohn mentioned. I appreciate that he was greatly handicapped in seeing the case today, because only scars remain.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by DR. ZEISLER.

A woman, aged 47, had an eruption of eighteen months' duration on the backs of the hands and elbows. The Wassermann reaction was negative. The basal metabolism was —10. There was no sensory disturbance. The skin in the affected areas was red, shiny and atrophic.

DISCUSSION

PROFESSOR JADASSOHN: This case is undoubtedly one of acrodermatitis atrophicans. This disease was rare in Breslau during the time in which I was assistant there. At present it is relatively frequent there. In the first case I saw in Breslau, many years ago, I made a diagnosis of scleroderma turning into an anetodermatic state of the skin. Now I believe that it was an acrodermatitis with a partial development into a sclerodermatoid type. The diagnosis of the earliest spots of acrodermatitis such as are seen on the shoulders of Dr. Zeisler's patient is very important.

I can make no suggestions for therapy.

DR. SULZBERGER: This disease is interesting, in regard to its regional occurrence and concerning the possible effects of climatic conditions, etc., on blastomycosis and coccidioidal granuloma. In Zurich the disease rarely occurs, and we did not see it frequently, while in Breslau I saw many cases. During three years in Zurich, I saw only two or three cases; one was in a patient coming from Germany, and, if I remember correctly, from a village not far from Breslau.

PROFESSOR JADASSOHN: I should like to add that Dr. Pautrier has also noted an increase of this disease in Strasbourg. Of course, we have no idea as to why there are these increases in frequency in different places and in different years, but we cannot believe it is merely coincidence. We have made many examinations of the endocrine organs, and for Abderhalden's ferments, without result (unlike our results in scleroderma).

MULTIPLE EPITHELIOMAS. Presented by DR. ORMSBY.

A patient, aged 44, with a disorder of one year's duration, was shown on account of the fact that the lesions were rather numerous, some presenting a benign cystic epithelioma type, others the ordinary basal cell type, while one of the lesions was distinctly different from either of these. There were three pea-sized, crusted ulcers, with rolled, pearly margins, situated over the right zygoma. There were several matchhead-sized lesions with translucent, firm, pearly borders, situated on each lower lid, and one on the right upper lid. Three similar lesions were found between the eyebrows, with telangiectatic vessels on their borders. There was one pinhead-sized early lesion on the left side of the forehead. A split pea-sized lesion was situated on the nucha, and a matchhead-sized one behind the right ear. Several pinhead-sized, firm, translucent, papules were present on the right side of the nose. In the left axilla, there was an almond-sized, raised, fungating nodule which was firm to the touch and the surface of which was reddish and crust covered.

DISCUSSION

PROFESSOR JADASSOHN: I believe that this is a case of Brooke's epithelioma cystica multiplex, but the lesions are not as numerous or as symmetrical as in some cases. The cysts are usually more pronounced in typical cases of Brooke's disease.

I cannot make a diagnosis of the axillary lesion without a histologic examination. It might be a case of Bowen's disease in a later stage or of the Darier's mixte or intermediaire cases of epithelioma of the skin. It cannot be decided whether or not there is any relationship between this lesion and those of the face.

DR. ORMSBY: The interest in this patient lies in the fact that the major portion of the lesions are of the type seen in multiple benign cystic epithelioma (Fordyce) but that they are of only one year's duration. Professor Jadassohn's discussion covered this point. The axillary lesion is probably of a different nature. A histologic examination will be necessary to decide its nature. Multiple benign cystic epithelioma usually begins in childhood. It originally was described by Fordyce and, independently, by Brooke. It is of much interest, therefore, to see lesions apparently of this type beginning in an adult and associated with other types in the same patient.

TUBERCULOSIS VERRUCOSA CUTIS. Presented by DR. WEIN.

This man was first presented at the April meeting of the Chicago Dermatological Society, and his history is recorded with the minutes of that meeting in a previous issue of the ARCHIVES.

Tubercle bacilli had been found in smears from the lesion; physical examination of the chest had revealed fibroid phthisis. Examination of the sputum was negative for tubercle bacilli, proctoscopic examination showed no pathologic condition in the lower bowel and smears were negative for tuberculosis.

DISCUSSION

PROFESSOR JADASSOHN: In this case I was especially interested in the small papules around the ulceration. They reminded me of a rare form of plane papules, resembling those of the so-called lichen scrofulosorum planus, which are sometimes localized around a lupus vulgaris. Similar papules exist also in tuberculous elephantiasis, and sometimes tuberculous tissue is found in them, and sometimes it is not found.

PSORIASIS (VEGETATING). Presented by DR. STILLMANS.

A negro barber, aged 58, was first presented before the Society in 1925, with an exudative, vegetating eruption of psoriasis of the flexor surfaces. This cleared up under the application of chrysarobin, but it had recently recurred. There was also leukoplakia of the palate and cheeks. He had had glycosuria for the past eight years.

At presentation the lesions consisted of nodules and tumors 0.5 to 5 by 3 cm., elevated 1 or 2 mm. and covered by brown crusts which could be peeled off, leaving a rough surface which fitted the projections on the under surface of the crusts and showed bleeding points. Only two lesions on the shaft of the penis were scaly. The axillae and groins were chiefly involved, but there were numerous lesions in the scalp and a few on the trunk and extremities.

DISCUSSION

PROF. JADASSOHN: This case of psoriasis would be very interesting, even in a white man, on account of the unusual microrupioid form.

DR. MICHELSON: It is a common observation that psoriasis is rare in the colored race, but in looking over my notes, I find that I have seen three cases of psoriasis of the ordinary type in negroes.

AMERICAN DERMATOLOGICAL ASSOCIATION

Clinical Meeting, San Francisco Hospital, San Francisco, July 1, 1929

LINGUA NIGRA. Presented by DRS. ALDERSON and WAY.

The patient, a man, a musician, first noticed during May, 1929, that his tongue felt rough, and there appeared to be a yellow tinge to it. The color had gradually become darker and the tongue rougher. There was some difficulty in speaking, and the tongue was more or less tender. The patient played a horn in an orchestra, and the condition interfered with his work. The family physician had prescribed hydrogen peroxide locally and some form of liver pills internally.

The entire dorsum of the tongue was covered with numerous, thin, filiform projections, which were intensely black. Many of the hairlike projections were fully 1.5 cm. long.

A fungus growth found in other cases by Weidman and Way and believed to be the cause of the disease could not be demonstrated in this case, although various forms of mediums were used. A growth of one of the common yeasts was repeatedly obtained, a nonchromogenic variety, which was not regarded as a pathogen.

DISCUSSION

DR. WAY: The trouble involving the tongue was first noticed about May 1, and within a week or ten days the entire dorsum was covered. When I first saw the patient, the filiform growth was from one-fourth to one-half inch in length. Cultures were negative for *Monilia*.

ATROPHY OF NAILS. Presented by DRS. MORROW, MILLER and TAUSSIG.

L. C., American born, aged 35, presented an atrophy of the finger-nails of seven years' duration. There was no history of any of the other members of the family being similarly affected. No fungus had been found in material from any of the lesions. The Wassermann reaction was negative; the general health was good.

Practically all the finger-nails were absent, and the toe-nails were markedly thickened.

Local and glandular therapy had had no effect on the course of the disease.

TELANGIECTASIA (FOLLOWING "TRICHO-SYSTEM" THERAPY OVER FOREARMS). Presented by DRS. MORROW, MILLER and TAUSSIG.

A woman, aged 36, American, presented a diffuse telangiectasia, with little atrophy, over the extensor surfaces of both forearms. The condition was of about one year's duration. The patient stated that she had received twenty or more "Tricho" treatments during the past two years for the removal of superfluous hair. Despite the extensive telangiectasia, the hair was as abundant as ever.

DISCUSSION

DR. ORMSBY: I think it is worth while to call attention to this case because it is a result of Tricho-system therapy, with telangiectasia.

DR. HOWARD FOX: We are all seeing the ill effects of roentgen therapy in hypertrichosis at the hands of advertising quacks. In order to fight this form of quackery we should send information concerning the bad results we see to Dr. Arthur J. Cramp of the Bureau of Investigation of the American Medical Association. We are trying to do this in New York, but many cases observed are not reported.

A CASE FOR DIAGNOSIS. Presented by DR. NORMAN EPSTEIN.

L. G., Portuguese, aged 65, presented several pigmented macular lesions, fairly symmetrically placed over the temples, behind the ears, sides of face, back

of the neck, chin and upper lip. They were a deep, bluish black, were non-infiltrated and had a tendency to enlarge peripherally. Aside from a moderate amount of pruritus there was no subjective symptom. The condition had been present for about ten months.

There was a history of the ingestion of drugs during the past year; i. e., sulphur bitters, cascara and Feenamint tablets; no bromide or iodide had been taken. Phenolphthalein, about 1.5 grain (0.097 Gm.) to the tablet, is present in Feenamint.

Physical examination gave negative results except for the condition of the skin. The spleen was not palpable. The urinalysis and Wassermann reaction were negative. The blood count showed 4,870,000 red cells and 7,200 white cells.

Biopsy showed a marked deposit of pigment in the upper corium, with a slight cellular infiltrate.

DISCUSSION

DR. PUSEY: I see over Dr. Lane's shoulder that he has a memorandum that it is a phenolphthalein eruption. I have had a strikingly similar case under observation in which the pigmentation is somewhat less marked, and there is some erythema beyond the patches, and I have thought my case was possibly an odd lupus erythematosus. I did not make this diagnosis in the case we are discussing, and accept Dr. Lane's diagnosis, but I think the possibility of lupus erythematosus is worth suggesting.

DR. HOWARD FOX: Has the patient been given phenolphthalein as a test to see whether the lesions would flare up, as they frequently do?

DR. LANE: This appears to be a phenolphthalein eruption.

DR. DENNIE: Antipyrine will produce the same fixed cutaneous lesions as phenolphthalein.

DR. MACKEE: I would suggest phenolphthalein eruption as the probable diagnosis.

Regarding the sensitivity test, sometimes a patient will not develop a phenolphthalein eruption on one occasion and will on another; so the test should be repeated over and over.

PROF. JADASSOHN: Antipyrine produces, as is known, eruptions similar to those produced by phenolphthalein. In Germany we more frequently see the antipyrine exanthems than the disease caused by phenolphthalein. It occurs sometimes only after years of use, and in some cases the eruption reappears after each introduction of antipyrine, but the sensitization may also disappear. That is the same as with the fixed arsphenamine eruption. I cannot remember a case of a symmetrical fixed antipyrine eruption, except in the mouth and on the genitalia.

DR. POLLITZER: This case was so obviously one of phenolphthalein eruption that I would like to ask whether any one wishes to state the case against this diagnosis.

SARCOMA (KAPOSI). Presented by DRS. MORROW, MILLER and TAUSSIG.

A man, aged 60, an American, presented purplish, infiltrated plaques, varying in size from that of a pea to that of a lima bean, over the backs of the hands, the upper surfaces of the toes, the angle of the right jaw and the lobes of the ears. The disorder was of two years' duration. It had been asymptomatic, new lesions developing from time to time.

Biopsy revealed dilatation of the blood vessels, infiltration of spindle cells and the presence of considerable pigment, as is seen in idiopathic multiple hemorrhagic sarcoma.

SARCOMATOSIS (MULTIPLE, HEMORRHAGIC-KAPOSI). Presented by the UNIVERSITY OF CALIFORNIA.

An Armenian, aged 77, was first seen in the clinic in September, 1920, when he had lesions of the hands, forearms, penis, legs and feet, of two or three years'

duration. The lesions varied in size from that of a pea to that of a lima bean; all had elevated borders, were palpable and doughy, and a few might have been considered infiltrated. They were purplish in hue and did not pale on pressure.

A biopsy from the skin over the external malleolus of the fibula made possible a diagnosis of Kaposi's disease. He had received radium and roentgenotherapy.

SARCOMATOSIS (MULTIPLE, IDIOPATHIC, HEMORRHAGIC-KAPOSI). Presented by DR. ALDERSON and DR. WAY.

An Italian fisherman, aged 60, stated that his present trouble began in 1920 in the form of small, purplish nodules on the inner side of the right calf, which disappeared spontaneously in a few weeks. Late in 1925, while in Alaska, a walnut-sized nodule appeared in the right thenar region. This was excised but not examined. In September, 1926, a few small, purplish nodules appeared on the medial three fingers of the left hand, and a few on the right hand; also, on the scrotum and on several toes. None of the lesions was painful, but they burned and itched. In November, 1926, he presented typical bluish nodules of this disorder scattered over the body and extremities, including also the scrotum, penis, mucosa of the lips and the area behind the ears.

The patient's general condition remained good. Several complete and differential blood counts were negative, and there were several negative Wassermann reactions on the blood. Tests for function of the liver were negative. The sputum was mucoid and showed many streptococci and staphylococci. Roentgenograms of the spine and fingers showed "definite fringing characteristic of Type II arthritis."

Cultures of material from extirpated lesions gave negative results, as did cultures on Sabouraud's mediums. Animal inoculation also was negative.

The patient had received several roentgen treatments.

DISCUSSION

DR. ALDERSON: The last patient in this group from the Sanford Service, whom I think many of the members did not see, has been treated recently by Dr. Epstein by roentgenotherapy. Comparison of the lesions now with what they were a year ago shows great improvement after only a few treatments. Will Dr. Epstein please give the dosage administered?

DR. EPSTEIN: The patient has had about four or five suberythema doses of roentgenotherapy.

A CASE FOR DIAGNOSIS. Presented by DRS. MORROW, MILLER and TAUSSIG.

W. J. H., aged 29, had turkey-egg-sized areas lighter than the normal skin on each side of the neck, which had been present for six years. There were no symptoms. The patient stated that the first area developed after a mosquito bite.

DISCUSSION

DR. WILE: The lesion impressed one at first glance as some form of nevus anemicus, and yet when I examined the biopsy carefully in Dr. Morrow's office, there was a peculiar yellowish tint, not only in the lesion itself but outside of the lesion, which led me to believe that there was some unusual connective tissue degeneration, something like an unusual form of colloid degeneration. This is my impression.

DR. PUSEY: I think this case should not go by as peculiar degeneration of the skin. It seems to me that it is a case of vitiligo on the side of the neck where we usually see it. The waxy color is that of the usual mottled vitiligo in that location.

DR. LANE: Dr. Wile suggested nevus anemicus. I do not see anything in the lesion which resembles nevus anemicus. In nevus anemicus there is absence of color in the lesions with no exaggeration of color at the borders. The skin at the borders may be slightly telangiectatic but is otherwise normal.

PROFESSOR JADASSOHN: I believe also that it is a vitiligo. The vitiligo is not always complete but some times there are lighter brown spots in the white spots. It is also occasionally seen that in the spot of vitiligo a light pigmentation returns, and in this way I think this case could be explained. It is also possible that a mosquito bite was the provoking factor, as we see provocation through pressure, e. g., of a truss.

KERATODERMIA PALMARIS ET PLANTARIS. Presented by DR. TEMPLETON.

A steamfitter, aged 27, first noticed a thickening of the palms and soles when he was 10 years old. There was no history of a similar condition in his family and no history of syphilis or the ingestion of arsenic.

The Wassermann reaction was negative; the basal metabolic rate was —20. Thyroid treatment and roentgenotherapy had produced no improvement.

EPITHELIOMA (MULTIPLE, BENIGN, CYSTIC). Presented by the UNIVERSITY OF CALIFORNIA.

H. N., a white woman, aged 53, was first seen in the clinic in September, 1928. At that time there were about a dozen firm, from pea to lentil sized nodules, pearly in color and telangiectatic, distributed over the central portion of the face near the nose. These lesions had been present for about twenty-two years and had remained symptomless.

The patient did not want any treatment.

MOLE (PIGMENTED, HAIRY AND VERRUCOUS). Presented by DR. E. K. STRATTON.

E. B., aged about 5, was first seen in May, 1925, at the age of 10 months. At that time a black, pigmented and hairy mole, approximately 6 inches in diameter, involved the left ear, left side of the face and scalp. On the face it extended to

Appearance of pigmented, verrucous and hairy mole when patient was first seen.

within one-half inch of the nose, encircling the outer canthus of the left eye. Several areas were verrucous, particularly in the region of the zygoma and the lower third of the ear.

The growth was destroyed by electrocoagulation in five stages.

A Case for Diagnosis. Presented by Dr. H. J. Templeton.

A Chinese housewife, aged 24, first noted a thickening of the palms and soles when 11 years old. The condition remained localized until the fall of 1928, when she noted an extension of the process up to the forearms. When seen by Dr. Templeton in November and December, 1928, the palms and soles were in the same condition now presented. Involving the forearms, knees, elbows, back and neck, there were large, sharply marginated, slightly roughened, brown areas of dermatitis, only slightly pruritic.

The Wassermann reaction of the blood was negative. Scrapings and cultures from the lesions on the body and extremities were negative for fungi. Roentgen therapy produced no improvement. At that time the patient was presented before the San Francisco Dermatological Society, but no diagnosis was reached.

Because of menstrual irregularity the patient was empirically placed on heavy doses of ovarian substance and thyroid. Since instituting this therapy the eruption had retrogressed until the hands and feet alone showed involvement. On account of a few spiny lesions on the wrists and dorsum of the fingers the diagnosis of pityriasis rubra pilaris was being considered.

DISCUSSION

Dr. MacKee: I think it is a case of pityriasis rubra pilaris.

Professor Jadassohn: That was my diagnosis, without any doubt.

Dr. Templeton: That was the tentative suggestion in the history.

Lichen Scrofulosorum. Presented by Dr. E. K. Stratton.

A girl, aged 13, had been under the care of Dr. Philip Pierson since Feb. 19, 1929, at which time she complained of periods of fatigue lasting from two to three weeks at a time, occasional night sweats, cold extremities and extreme loss of weight. She had no fever, colds or cough. Dr. Pierson's positive physical observations, including roentgenograms, showed the patient to be 25 per cent underweight, flat-chested, and with thickened hilus glands. He obtained a positive cutaneous tuberculin test and made a tentative diagnosis of lymphatic tuberculosis. During this observation he noticed a few groups of skin lesions scattered here and there, and referred the patient to Dr. Stratton on April 23 for an opinion.

On the flexor surface of the wrists, around the elbows, knees, ankles, axillae, and the inner surface of both thighs, were groups of discrete, lichenoid, reddish papules, presenting no subjective symptoms.

No specific treatment had been centered on the skin lesions, but under alpine light treatment for the general condition, rest, diet, etc., the patient had gained 12 pounds (5.4 Kg.) and felt much better.

DISCUSSION

Dr. Williams: I think there is no doubt that this patient has tuberculosis. She also has lichen lesions, but I think they have nothing to do with the tuberculosis. I think it is a characteristic case of lichen planus occurring in a tuberculous patient.

Aphthous Stomatitis (Chronic) Periadenitis Mucosa. Presented by Dr. Norman Epstein.

E. J., a white woman, aged 37, complained of recurring sores in the mouth. There was no history of other members of the family being similarly afflicted. The patient recalled that during her girlhood she had occasional canker sores, and

since the age of 20 she had had almost constantly recurring ulcerations on the tongue, gums, buccal mucosa and inside of the cheeks. The ulcers varied in size and depth, and healed spontaneously, leaving a scar.

Physical examination was negative except for the scarring of the oral mucous membranes, and the ulcerations. Hemogloblin was 90 per cent.

Treatment had been ineffective.

DISCUSSION

DR. WILE: I think that periadenitis is a poor descriptive term for an unusual condition that occurs in the mouth. I think this is the second case I have seen of ulcers that occur on the tongue and sometimes on the gum and lip, always leaving scars.

PROFESSOR JADASSOHN: I believe this is the disease we call "aphthae resistantia," but of course we know that it has nothing to do with aphthous stomatitis. The disease is not rare especially in private practice. According to my personal experience in Berne and Breslau the disease is perhaps more frequent in women than in men, and I know some cases in several members of the same family. The disease can exist for many years, or even throughout life. It is otherwise benign. Some people have such irritations all the time, some times many lesions and some times only a few, but they are never really free from such eruption. In other instances, the eruption is intermittent. I know of one young woman who had the eruption for many years and then was free for two years after arsenical treatment; she believed she was cured, but the eruption recurred. Some authors believe there is a relation between this disorder and trouble in the stomach. Many persons are made unhappy by this disease and have much pain, especially when the eruption comes out. The only treatment that I believe can sometimes influence it for prolonged periods is internal arsenical treatment. Some times the spots are healed with scars, but much more frequently without.

DR. ORMSBY: It is interesting to hear the discussion of Professor Jadassohn in this case. This particular disorder was first reported almost simultaneously abroad and in this country. It is therefore of interest to us to find that our European colleagues agree with us on the important points in these cases. They are not common and are exceedingly resistant to treatment. Arsphenamine has been praised, and we have used it with success in two or three instances. In the others it was of little value. The lesions in some of these cases become rather deep and last for a longer time than was described in the original reports. The name given the disorder in this country was suggested on account of the involvement of the mucous glands in the process.

DR. HOWARD FOX: The two points brought out that this disorder is rare and persistent were well demonstrated by the case I showed Professor Jadassohn in New York. None of my colleagues had apparently seen a case just like that one. The patient had been previously treated with sodium biborate locally and with arsphenamine intravenously without any benefit. Vincent's angina and tuberculosis had been excluded by bacterial examination. I have tried roentgenotherapy recently, with marked improvement.

DR. MACKEE: I understand that true cases of periadenitis begin as a nodule followed by ulceration. I have seen a number of cases of aphthous stomatitis with exacerbations of ulcers over a period of many years. I have not looked on those cases as periadenitis because the lesions do not begin as nodules. This patient says her lesions all start as nodules, and I think the case can be labeled periadenitis. Fordyce and others who have studied these cases carefully consider them to belong to the papulonecrotic tuberculids.

DR. PUSEY: I wish to express my appreciation of having aphthous stomatitis restored to good standing, rather than periadenitis necrotica. These cases are rare, and I have a distinct feeling — the only place in which I differ from Professor Jadassohn — that they are associated with gastro-intestinal disturbance. I have patients who develop these lesions after eating certain kinds of food, one from tomatoes, for example. They cause scars or they do not cause scars, according to the depth of the lesion.

DR. SHELMIRE: We have had two or more cases of this type under our observation in Texas. A typical one occurred in a physician, who had suffered for several years. Most of the lesions begin as distinct nodules, break down into necrotic ulcers, and some take two or three months to heal, leaving distinct scars. I think Dr. Michael had made the diagnosis in the case of the physician to whom I refer. We have found no treatment effective.

DR. MORROW: I wish to agree with Dr. Pusey, but the condition is not so rare as many think. During the last few years Dr. Miller and I have seen at least half a dozen cases, all with scar-leaving lesions. Another thing that has not been emphasized is the family history. Two children in one family have been coming to the clinic for a long time, and neither of them has improved under arsphenamine therapy or anything else. The groups of nodules appear intermittently. The members of another family coming to the office at the present time give a history of lesions that leave scars. In one case the lesions have been appearing since childhood, and the patient is now about 30 years of age. The mild type of lesions is indistinguishable from the canker sores. The woman's mouth is literally filled with scars from deeper lesions she has had in the past. She gives the history of her brother having had similar lesions and of similar lesions appearing in other members of her family.

SENSITIZATION TO SUNSHINE. Presented by DR. TEMPLETON.

This infant had presented no lesions on the skin up to the age of 10 months. At that time she was exposed to bright sunshine daily for two or three days, and immediately afterward her mother noticed an intense dermatitis on her face. The dermatitis soon faded but reticulation remained. One month before presentation following exposure to sunshine the skin of the extremities went through the same process, and was followed by reticulation of the same type. No ingestion of drug preceded the onset of the dermatitis and there was no history of a similar condition in the family. The mother stated that the child had passed worms.

It was thought that xeroderma pigmentosum should be considered as a possible outcome in this case.

DERMATITIS FACTITIA. Presented by the UNIVERSITY OF CALIFORNIA.

M. S., a white woman, was first seen in the clinic in June, 1929, because of lesions on her extremities. When presented she had extensive, excoriated lesions over both legs and arms, most marked on areas easily reached by the right hand. The patient stated that the first lesion appeared at the age of 11 years when there was an abrasion on one leg, following a slight accident. Since then she had scratched her arms and legs almost continually because this relieved the burning and itching sensation. She had always been nervous. She had been married for five years, and had two spontaneous abortions, at three and six weeks. There were extensive operative scars over the extensor aspect of each thigh, from an attempt to remove the affected areas surgically. Physical examination gave negative results. Laboratory observations were negative except for a basal metabolic rate of 11.9.

The patient had been continually under treatment for the skin condition for years, receiving courses of carbon dioxide snow, radium, ultraviolet light, ointments, arsphenamine, electric needles, etc.

A plaster of Paris cast was applied over the affected areas, and ten days later when it was removed, the skin under it was normal.

DISCUSSION

DR. MACKEE: Neurotic excoriations may produce this picture, but there are some features that lead one away from that diagnosis. The definite grouping and the fact that many of the lesions are nodules, which might be secondary but might also be primary, and also the exceedingly intense and persistent itching speak for prurigo nodularis rather than neurotic excoriations. Dr. Morrow has

had the patient under observation for a long time, and believes the lesions are entirely due to trauma. I am not willing to accept unequivocally the diagnosis, because in neurotic excoriations the scratching and picking are not caused by itching, but because the patients are convinced that there is something in the tissues which must come out. There may be various local sensations which are temporarily lessened by picking. The patients readily admit an uncontrollable impulse to dig into the skin.

DR. KETRON: The patient stated that she got relief after she made the lesions bleed.

DR. MICHAEL: I had in mind prurigo nodularis for a long time, and still have. In addition to the points Dr. MacKee made, I think that the fact that the lesions have recurred in the stitch marks is in favor of prurigo nodularis. Against my advice the patient went to a surgeon and had some of the lesions excised.

DR. CRUTCHFIELD: I saw this woman when she first developed the lesions. I thought it was a case of prurigo nodularis, but did not have the courage of my convictions and submitted specimens from a biopsy to Dr. Highman. That was his diagnosis. I think it probably is a case of prurigo nodularis.

PROFESSOR JADASSOHN: I believe it is possible to take both these diagnoses together. I find no difficulty in saying that eruption in the form of prurigo nodularis can be influenced by psychic factors. We know that psychic influences can also change the secretions of all glands, and in this manner it can be explained that an urticaria or even a form of a prurigo nodularis disappears under psychic influences.

DR. POLLITZER: I should like to ask if any one who has seen this patient over a long period has seen a lesion that he would call prurigo nodularis before it was all scratched up. To me it is conceivable and indeed probable that the infiltration we now find is secondary to the scratching. It is also striking that this prurigo nodularis has had the peculiar fancy to locate itself where it is easiest to scratch.

DR. MILLER: As a therapeutic measure we intend to put a plaster of Paris cast on the arms and legs of this patient. We have never observed any lesions which were those of prurigo nodularis. All lesions have been scratched and irritated.

DR. WILLIAMS: I think this case is not prurigo nodularis. The cause is not yet determined, but cases which I have seen have separate nodular lesions some of which show no scratch marks. I did not find any such lesions in this case but rather a pruritus of long standing.

SCLERODERMA. Presented by the UNIVERSITY OF CALIFORNIA.

Mrs. G. A., white, aged 36, entered the University of California Hospital on May 6, 1929, because of hardening of the skin with brawny pigmentation of one year's duration.

The patient was well until about two years before presentation when her hands began to swell and become blue and stiff with changes in temperature. She had much gastric distress at this time, and a physician advised operation. In 1927, the appendix, hemorrhoids and an ovarian cyst were removed and the gallbladder was drained. There was no relief from the symptoms, and about a year later she noted that the skin on her chest was becoming drawn. There had been increasing weakness and a loss of 50 pounds (22.7 Kg.) in weight during the past two years. The skin over the entire body had gradually become pigmented, and other joints had been growing stiff and painful. During the last six months the pigmentation had increased rapidly, menstruation had been scanty and there had been marked increase in the growth of hair over the body and scalp.

Physical examination was negative except for fulness and resistance on palpation over the epigastrium on the right. Motion was definitely limited in all joints, the hands and feet were cold, the muscles weak, and the reflexes hyperactive.

The blood pressure was 86 systolic and 76 diastolic, erythrocytes 2,700,000, and hemoglobin 70 per cent. The basal metabolic rate was 8.6 plus. Tuberculin tests were negative. There was no change in the creatine.

The patient had received suprarenal extract (McLean-Kochler), one capsule three times a day, since June 4, 1929. There had been no increase in pigmentation during the past month, and she thought she felt somewhat stronger. The blood pressure remained unchanged.

LUPUS VULGARIS. Presented by DR. ALDERSON.

This patient had the ulcerating form of this disorder and was treated for four years with rest in bed, tuberculin, arsenicals, ultraviolet light and roentgenotherapy without benefit, the lesions being steadily progressive.

He was then placed on treatment with gold sodium thiosulphate, 100 mg. once weekly for fifteen doses, then a period of two weeks' rest, when treatment was resumed. In all, forty-five doses had been given, and the condition showed marked improvement.

HANSEN'S DISEASE (NERVE TYPE). Presented by the UNIVERSITY OF CALIFORNIA.

L. V., a Mexican woman, aged 27, born in Mazatlan, was first seen in the clinic in August, 1928. She had noticed changes in her finger-nails eight years previous to presentation, and a pigmented area on her back. As a child she had several dollar-sized erythematous lesions on her forehead, chest and thighs, which lasted several years. Scrapings from her finger-nails had been negative for fungus on two occasions. Cultures from the nose had been negative for Hansen's bacillus.

For the last year she had received weekly, intramuscular injections of chaulmoogra esters, 3 cc., and had taken potassium iodide in increasing doses up to 240 grains (15.5 Gm.) twice a week.

A CASE FOR DIAGNOSIS: HANSEN'S DISEASE (?). Presented by the UNIVERSITY OF CALIFORNIA.

N. S., a negress, aged 29, was first seen in the clinic in June, 1929, because of a lesion on the back of the left hand which had been present for one year. A definitely palpable, slightly elevated, depigmented area, 1 cm. wide, extended across the hand near the wrist. There was slight tenderness and itching, no pain, and no change to hot and cold. There was slight hyperesthesia. The Wassermann reaction was negative.

Biopsy was suggestive of leprosy, but no bacilli or vacuolated cells were found.

The family and past history were negative, except that the patient had lived in Louisiana for several years.

The patient complained of daily headaches and general listlessness, with pain in the back and thighs, and of painful micturition with hematuria.

Physical examination was negative except for tenderness in the right lower quadrant and over the symphysis. The urine was positive for sugar. The wall of the bladder was injected with Hunner's ulcer in the upper quadrant, and there were two large polyps in the neck of the bladder.

HANSEN'S DISEASE: MIXED TYPE. Presented by DR. CHIPMAN.

A. C., a man, aged 21, born in Tahiti, gave a history of bronchitis at the age of 10 years, but had had none of the usual diseases of childhood and no previous skin disease. He presented an eruption which began eight months previously on the posterior aspect of the right arm, slightly above the elbow. Two or three months later superficial, slightly pigmented (fawn colored) areas, with slight scaliness, developed on the face, arms and thighs; then nodules varying in size from that of a pea to that of a walnut appeared on the face, arms and thighs. Six months before presentation he had an ulcer of the cornea.

Microscopic examination of smears of serum from the nodules showed Hansen's bacilli.

DISCUSSION

DR. ERNEST WALKER, San Francisco: I am not a dermatologist but have been interested in leprosy for a number of years. In 1927 and 1928, through the courtesy of the United States Public Health Service, I spent some time in investigating the epidemiology of leprosy in Hawaii. As dermatologists you know the confusing condition of the pathology of this disease. Since Hansen discovered the bacillus, little progress has been made. All attempts to culture the organisms have been considered negative. Various bacteria have been cultivated. Rarely are these acid-fast, they do not resemble Hansen's bacillus in the tissues, and they are generally considered as contaminants.

The general opinion has been held that Hansen's bacillus is a parasite so exactly adapted to its host that it cannot be cultivated on artificial mediums. In Hawaii I confirmed the work of others that we cannot cultivate anything which is identical with the organisms found in the tissues, but that we can cultivate other organisms, which usually are not acid-fast, and which are of variable morphology.

I have felt for a number of years that the solution of the etiology of leprosy lay in the interpretation of the forms we are able to cultivate. Other investigators have previously suggested that this was the case. I have been able by using a great variety of mediums to prove that each of these morphologic types cultivated from leprosy can be transformed one into the other, and that we can make them acid-fast or acid-sensitive at will. The conclusion was reached, and I think justifiably, that all these cultivated forms of leprosy are in the life cycle of one organism.

The question arises as to what this organism is. A careful study of the organism has shown that it is an actinomyces, one of the group lying intermediate between the fungi and the true bacteria. So the suspicions of earlier investigators seem to be fairly well established by cultural means.

The next question would be to prove that this cultivable organism is the cause of leprosy. As you know, the proof of the relation of Hansen's organism to leprosy rests on circumstantial evidence. We have not been able to satisfy the postulates of Koch, since we are unable to inoculate successfully man or animal with the organism. In the cultural organism we are confronted with the same conditions. I turned to the rat as the most promising experimental animal. As you know, since 1903, when the rat leprosy was discovered, we have known the disease was similar to human leprosy. It is principally the skin type of lesions, and enormous numbers of acid-fast bacilli are found, similar to those of leprosy in man. The general opinion has been that rat leprosy is similar to leprosy in man, but nevertheless a distinct discase. I have been able to cultivate the same organism from leprosy in rats, and my study has convinced me that the disease is identical with that in the human being. This promises to throw much light on leprosy in man, and it seems to promise an experimental animal, without which we could not go much further.

In nature active rat leprosy with skin lesions occurs in a small percentage of rats. Investigation about San Francisco has shown, however, that about 65 per cent of them have latent leprosy in the spleen, and other internal organs. Therefore if we inoculate leprosy into rats what should we expect to get? Probably only one in thousands would develop active leprosy. We can infect the rats with our cultures, and can recover the organism in culture after a year; so we all but satisfy Koch's postulate. We have found all but the skin lesions, and would not expect that without experimenting with many thousands of rats. We have recently turned to experimentation on monkeys, but have not yet done enough work with them to report.

The question arises how leprosy is transmitted from man to man. Among the primitive races there is usually no fear of leprosy or thought of contagion. In the Middle Ages when leprosy was prevalent in Europe, there was great fear of the disease, and harsh laws were passed to protect people. Later it was

believed that it was an hereditary disease, or not infectious. This was believed so strongly that Danielssen inoculated himself and others repeatedly with leprous tissue, blood, and so forth, without any symptoms developing. With the discovery of the Hansen bacillus the idea was revived that the disease was contagious, and that is the opinion held today, that it is a feebly contagious disease; but examination of the evidence is none too convincing.

If we consider the biology of the leprosy organism it will, I believe, throw some light on the method of spread of leprosy. *Actinomyces* are saprophytes which live in the soil. This has suggested the possibility that leprosy may also be due to a facultative parasite. In Hawaii I made cultures of the soil and found I could cultivate an acid-fast organism in 98 per cent of the samples of soil collected throughout the Islands, and investigation showed that these were identical with the organisms which I had cultivated from leprosy. So it would appear, if my investigations are correct, that leprosy is primarily a soil infection, and the man becomes infected through wounds contaminated by these infective saprophytic *Actinomyces.*

If leprosy is due to this widespread soil organism you will say "Why do we not all have leprosy?" I have made a survey of the soil in the United States and find these organisms present throughout the whole country. My answer is, "Why do we not all have tetanus?" which is also caused by a widespread soil organism. The infection with both diseases depends on the habits of the persons, on the care they take of general sepsis, on wounds and many other factors. The most important practical application of this new knowledge is in connection with the control of leprosy. The civilized governments of the world are spending millions to segregate and isolate lepers, and the unfortunate victims are being taken from their homes and isolated from their families for the remainder of their lives. It may be found that this is not necessary, or at least only partially necessary, and that cases of leprosy do not need to be isolated except perhaps the far advanced cases; for I admit that while leprosy is primarily a soil infection, infection by direct contagion may occasionally take place. In all of the actinomycoses the disease is rarely if ever transmitted from man to man, but it usually comes directly from the soil. If my investigations are correct, I think we shall see new methods of handing lepers. The protection of the feet and the body against wounds, and the prompt disinfection of wounds may turn out to be more important than are the segregation and isolation of lepers.

DERMATITIS SEBORRHEICA (?). Presented by the UNIVERSITY OF CALIFORNIA.

A. R., a white woman, aged 56, was first seen in the clinic in October, 1921, because of a generalized dermatitis which had been present almost constantly for forty-six years. At the age of 9 her skin became dry and scaling, with pus under crusts on the face, neck, scalp and arms. Since that time the skin had remained thick and rough, with an almost continuous dermatitis. During the past fifteen years the condition had been extending over the body. The family history was negative except that her father died of "miner's consumption." The patient's general health had been good except for erysipelas at the age of 41.

On routine examination a fibroid uterus was found and a supravaginal hysterectomy was performed in 1923.

The laboratory observations were negative, including all skin tests.

Treatment had consisted of ultraviolet light, roentgenotherapy and local medication. The skin was almost clear from August, 1926, to August, 1927; then there was a recurrence over the face and chest and in the axillae, which responded slowly to a course of treatment with gold sodium thiosulphate, and slightly to sodium thiosulphate. The skin had been markedly improved during the last six months, though not entirely clear.

COCCIDIOIDAL DERMATITIS. Presented by the UNIVERSITY OF CALIFORNIA.

J. W., a man, aged 63, had lived in the San Joaquin Valley. His left leg was removed six years before presentation because of localized coccidiosis. Two

months after removal an erythematous dermatitis developed over each eyebrow and the left temple. It produced no symptoms and had remained localized to those areas for over five years. An occasional follicular pustule developed, from which many double contoured organisms with endospores could be demonstrated.

DERMATITIS HERPETIFORMIS. Presented by the UNIVERSITY OF CALIFORNIA.

O. S. W., a man, aged 31, had had a grouped, vesicobullous eruption for fifteen months. The lesions appeared in crops and involved the entire skin. They were accompanied by pigmentation and pruritus.

Treatment had consisted of the use of ultraviolet light and an animal-protein-free diet.

LUPUS ERYTHEMATOSUS: MARKED INFILTRATION OVER LEFT CHEEK. Presented by the UNIVERSITY OF CALIFORNIA.

M. K., a white woman, aged 60, presented an eruption which involved the left cheek and the nose. The eruption consisted of erythematous lesions with atrophic areas and follicular plugs, especially in the ears. There was considerable infiltration in the areas over the left cheek.

She had received eighteen intravenous injections of gold and sodium thiosulphate, 0.1 Gm. each, with only slight improvement.

SCLERODERMA (GENERALIZED). Presented by the UNIVERSITY OF CALIFORNIA.

C. C., a white woman, aged 27, was first seen in the University of California Hospital in 1917, with chills, fever and stiffness and edema of the skin. For several days there was a macular rash over the face and upper part of the body, with severe pruritus. The skin became stiff and thick with linear areas of warty dermatitis over the arms and thighs. This acute condition lasted for four weeks and was followed by complete recovery. In 1925, she was in bed for three months because of "rheumatism," and there was a recurrence of this condition in 1926, which persisted for three weeks.

The present condition began in December, 1928, two weeks before she entered the hospital on Jan. 6, 1929. The illness began as an attack of influenza. Nine days later red blotches appeared on the skin, and the stiffness began increasing rapidly, until when the patient entered the hospital her face was stiff and masklike. The thickness and stiffness of the skin extended over the entire body. There was no pitting on pressure, but a hard, boardlike rigidity. The fever lasted for eleven days.

Physical examination showed enlargement of the heart; a systolic murmur could be heard all over the pericardia. A skiagram of the heart showed a mitral outline.

The laboratory observations were negative. The basal metabolic rate on two occasions was 18 plus and 7 plus, respectively, during the time the patient had fever.

There had been slight gradual improvement. In the hospital the treatment had consisted of cerium oxalate, sodium salicylate, whole pituitary extract and amiodoxyl. Since returning to the clinic there had been little medication.

LYMPHANGIOMA CIRCUMSCRIPTUM OF THE TONGUE. Presented by DR. TEMPLETON.

A. M., a woman, aged 23, stated that the lesions on her tongue were first noted when she was about 3 years old, while she was living in Hawaii. There was no history of similar lesions in the family. The tongue was not painful but was sensitive to acids and highly flavored or seasoned foods.

A few of the lesions were destroyed with a fine pointed actual cautery. On puncture they collapsed immediately.

LYMPHATIC LEUKEMIA (TOXIC) WITH SKIN INVOLVEMENT. Presented by the UNIVERSITY OF CALIFORNIA.

V. H., a Spanish woman, aged 61, was referred to the clinic from the San Francisco Hospital in January, 1929, with a diagnosis of lymphatic leukemia with coincident skin lesions, diabetes mellitus and hypertension. Roentgen examination of the chest showed some calcified glands, small calcified shadows on the left behind the third rib. The lung fields were otherwise clear.

On Oct. 31, 1928, there were 250 mg. of dextrose per hundred cubic centimeters of blood; in April, 1929, 222 mg. In November, 1928, the blood count showed 39,950 leukocytes, small leukocytes 83 per cent; in June, 1929, 21,350 leukocytes, small leukocytes 60 per cent; mononuclears 2 per cent; basophils 1 per cent. The Wassermann reaction was negative.

Physical examination showed a dry, scaling, erythematous and thickened skin all over the body, lymphadenopathy, and a palpable liver. The blood pressure was 150 systolic and 70 diastolic.

The patient was placed on treatment with insulin, an appropriate diet, and roentgen therapy. Treatment for the skin consisted of ultraviolet light irradiations and local applications.

A biopsy specimen was presented.

LICHEN PLANUS OBTUSUS (?). Presented by the UNIVERSITY OF CALIFORNIA.

A. J., a woman, aged 57, came to the clinic in 1924 because of lesions on the nose and the extensor surfaces of the lower legs, which caused severe pruritus. The patient was rather vague as to the duration, but thought the irritation began during her last pregnancy at about the age of 40.

Over the anterior aspects of the lower legs were several dozen discrete, keratotic, lentil-sized papules giving the appearance of a nutmeg grater. The nose was erythematous, considerably enlarged and excoriated.

The family and past histories were unimportant. Physical examination and laboratory observations were negative.

Various kinds of medication had been used without relief, including roentgen therapy, ultraviolet light irradiation and the use of the Grenz ray.

Biopsy revealed a marked hyperkeratosis and a round cell infiltration around enlarged blood vessels. The bandlike infiltration seen in lichen planus was not present.

DISCUSSION

PROFESSOR JADASSOHN: We see these cases rarely; I believe that they belong to the group which is designated by Brocq as "Neurodermite chronique." We know that the "grosser papules" (Vidal) occur in all cases of the prurigo group. They can be exceedingly large, and I have the impression that after some time, when they are well developed they are still rough but are no longer scratched. Also, in this patient I had the impression of few scratch marks. We see this form more frequently on the extremities, particularly on the legs, than on the rest of the body. At the same time we see occasionally eruptions on the body, and these can be either the gross papules, or only small lichenoid papules. We know that between the cases that we call also lichen disseminatus (Vidal), and the disease called urticaria perstans by the Vienna school, forms of transition exist. All of these eruptions with their different names have transitional forms, because a large part of these dermatoses depends especially on the form of reaction of the patient.

SCLERODACTYLIA. Presented by the UNIVERSITY OF CALIFORNIA.

S. S., a white woman, aged 34, was born in the United States but lived in Syria between the ages of 1 and 13. She was a seamstress by occupation and came to the clinic in January, 1929, complaining of numbness and loss of feeling in her fingers and toes, with alternate blanching, reddening and burning. This condition had been present intermittently for twenty-one years.

Examination showed definite blanching of all the fingers, with marked tension of the skin, probably due to edema. There were no contractures and no changes in the skin. The nails were all normal. The family history was negative. The patient thought the condition began at the age of 13, when her toes were frozen. She received treatment for frost bite at home. There were no symptoms for two or three years after this episode, but then the fingers and toes both began to turn blue with cold, and to have sensations of burning and itching, alternating with numbness.

There was a history of a tonsillectomy at 21, and of rheumatism at 24; otherwise there had been no operations and no illnesses. She complained of "gas" pains, pain in the neck and nervousness.

The laboratory tests were all negative, including blood calcium, phosphorus and dextrose tolerance tests. Roentgenograms of the legs showed no calcification of the blood vessels. Those of the teeth revealed pyorrhea and an abscess of the second bicuspid.

Treatment had consisted of iodine petrogen locally, with parathyroid and calcium by mouth. The condition had remained practically unchanged.

LEIOMYOMA. Presented by DRS. MORROW, MILLER and TAUSSIG.

A. M., a French woman, aged about 55, first noticed lesions on her forearms thirty years before presentation. The lesions continued to increase in size and number until about five years previous to presentation. The large lesions were painful to the touch, especially in cold weather. They were scattered over the arms, forearms, chest, breasts, thighs, etc. Some of the larger lesions had been removed under anesthesia with procaine hydrochloride because of the pain they caused.

Biopsy revealed the characteristic observations.

DISCUSSION

DR. HOWARD FOX, New York: This case has the typical appearance of leiomyoma but lacks the characteristic tenderness of this disease. I recall two cases seen at the meeting in Bonn two years ago, in which ordinary handling of the lesions caused the patients considerable discomfort.

DR. MILLER: This is true at the present time but has not been true throughout the course of the disease. I have cauterized and removed many lesions because the patient complained of tenderness and pain in them.

DR. POLLITZER: It is worth emphasizing that the lesions began at about 34 and continued to occur until the patient was about 50, and that there have been no new lesions since that time.

MELANOCARCINOMA (GENERALIZED METASTASES). Presented by DRS. ALDERSON and WAY.

L. M., a woman, aged 66, who had always been plump and well nourished, started losing weight three years before presentation. She gave a history of having had pneumonia, arthritis, sciatica, two pulmonary hemorrhages, varicose veins with ulcer, frequent headaches and nose bleed, and several fainting spells during the menopause. Both parents had died of yellow fever. She had six children living and well; one son had several dark hued moles on his body.

In July, 1928, the patient first noticed a few black spots on the body and scalp. One month later she was found in bed unconscious and with a multiple generalized eruption, which was diagnosed purpura by her family physician. She was removed to the hospital and given a blood transfusion because of a severe secondary anemia. Improvement in the general condition followed, and the patient left the hospital in three weeks. The eruption persisted and was accompanied by periods of almost unbearable itching and skin sensitiveness. The itching was

so severe that the patient would tear her clothing off for relief. New lesions continued to develop from time to time, and the patient steadily lost weight and strength.

Physical examination showed marked emaciation, with multiple, brownish-black, flattened papules over the body. Her temperature was 96.8 F., blood pressure 165 systolic and 80 diastolic, pulse 80. The cervical glands were enlarged, as were the inguinal, and examination of the lungs revealed moist râles at the bases and patches of impaired resonance.

Examination of the blood showed hemoglobin 60 per cent, red blood cells 3,600,000, white blood cells 4,000. Differential count: lymphocytes 15, polymorphonuclears 77, transitionals 7, eosinophils 1.

The skin showed multiple, brownish-black lesions, round or oval in shape, from 1 mm. to several centimeters in size. They were distributed by the hundreds over the face, scalp, neck, chest, back, arms and legs, and to a slightly less extent on the thighs, buttocks, palms, soles, nail beds, ears, and the mucous membrane of the vagina, nose, eyelids, cheeks, throat, palate and conjunctiva. A cerebelliform pigmented mole, about 3.5 cm. in diameter, was seen on the back, which was believed to be the primary lesion. The patient stated that it was smaller and had the appearance of a blackberry for many years.

An elevated, pigmented nodule had been removed from the anterior surface of the right leg near the ankle. Sections were stained with hematoxylin-eosin and Pappenheim's stain.

Histopathology.—The stratum corneum was thickened, and many of the squamous cells showed a perinuclear vacuolization. A few of the interpapillary processes had disappeared; some of the epidermal cells next to the corium showed an increased pigment content. Most noticeable, however, was the thinning of the epidermis.

The malignant cells comprising a part of and infiltrating the corium displayed an extraordinary polymorphism; the prickles or protoplastic bindings, so characteristic of epithelial cells, were entirely lost. Many of the cells were deeply pigmented to the tips of their finely branching processes; so pigmented that often only a nucleus was visible. Some of the more mature cells had ruptured, scattering free pigment about.

The free pigmented cells were proliferating rapidly, at the same time retaining their polymorphism and long processes, and under high power many of them looked exactly like what they were, enlarged cells of the deeper layers of the epidermis which had become ameboid. As these rapidly proliferating cells reached the deeper layers of the corium, they arranged themselves in the dilated tissue spaces in an areolar manner, morphologically resembling an acinar tumor. Noticeable was the lessening of the pigmentation as the deeper layers were reached, for the young cells had not yet gained the power of producing pigment.

Pigmented, branching or rounded cells with globular pigment masses could be seen even in the deeper layers within the fibrous tissue septums, but these could be recognized as phagocytic cells which had been carried by the lymphatics from the upper portion of the tumor. Lymphocytes, plasma cells and mast cells occurred with varying frequency throughout, and characterized the process as one of a chronic, inflammatory type.

Morphologically, the sections represented a metastatic, melanotic epithelial tumor of more than moderate malignancy.

DISCUSSION

DR. ALDERSON: This patient's condition speaks for itself. The notes are complete, and the report with photographs (gross and microscopic) will be published shortly. Probably in a few weeks a postmortem report will be added.

DR. STUART C. WAY: The case is interesting because of the history of the onset. The patient claims she has had for many years a pigmented mole near the center of her back; sometime ago a few lesions appeared in her scalp, and that soon after this they found her unconscious one morning, covered with the present lesions. They were at first very much like purpura hemorrhagica, but recently have become more pigmented.

KERATOSIS FOLLICULARIS (DARIER'S DISEASE). Presented by DR. C. E. SCHOFF.

A woman, aged 22, had a disorder which first involved the temples, scalp, base of neck and axillae at the age of 8 years. The family history was negative as to skin diseases. She was first seen by Dr. Schoff on May 20, 1920, when she was 13 years of age.

The scalp, face, neck, flexures of forearms, and extensor surfaces of the lower legs were the sites of hyperkeratosis follicularis.

The urine and Wassermann reaction were negative. Physical examination was negative except for an adenomatous thyroid.

She had been treated locally with keratolytic ointments, and had received roentgen therapy and thyroid extract.

Biopsy of the skin of the leg revealed diffuse thickening of the horny layer. In places the horny masses were piled up in thick layers, some of which were lifted off from the epidermis by collections of clear fluid or blood. There were a few degenerated cornifying cells in the epidermis, and heavy pigmentation of basal cells. There was no round cell infiltration in the cutis.

KERATOSIS FOLLICULARIS (DARIER'S DISEASE). Presented by DR. C. E. SCHOFF.

A girl, aged 10, gave a history of an eruption beginning at the age of 7, which was localized about the base of the neck. It persisted for a time and disappeared, to recur a few months previous to presentation. Her general health had always been good, and physical examination did not elicit any pathologic change aside from the skin condition.

Examination of the blood showed: red blood cells, 5,070,000; white blood cells 12,850; hemoglobin 75 per cent; color index, 0.75. Differential count showed: polymorphonuclears, 49 per cent; lymphocytes, 36 per cent; mononuclears, 1 per cent; eosinophils, 1 per cent; basophils, 2 per cent, and transitionals, 1 per cent. Morphology was normal. The blood sugar was 114.2 mg. per hundred cubic centimeters of blood; blood urea 25 per hundred cubic centimeters of blood, and blood urea nitrogen 11.7 per hundred cubic centimeters of blood. The Wassermann and Kahn tests were negative.

Biopsy section submitted showed keratosis follicularis.

KERATOSIS FOLLICULARIS (DARIER'S DISEASE). Presented by DR. C. E. SCHOFF.

A widow, aged 31, mother of the preceding patient, gave a history of having the usual diseases of childhood, and of a tonsillectomy and appendectomy in 1921. She also had paroxysmal attacks of otitis media and of metorrhagia for several years. Her family history was negative except that her mother and one sister had a similar condition of the skin.

The disease began about the base of the neck and the axillae at about the age of 7, gradually spreading over the entire upper torso.

Physical examination did not elicit any clinical pathologic change of importance other than the condition of the skin, except a secondary anemia, probably due to a metorrhagia from a fibroid uterus.

Blood examination showed: red blood cells, 2,795,000; white blood cells, 11,300; hemoglobin, 34 per cent; color index, 0.7. Differential count revealed: polymorphonuclears, 70 per cent; lymphocytes, 25 per cent; mononuclears, 2 per cent; eosinophils, 1 per cent, and basophils, 2 per cent. Morphology: The red blood cells showed marked variance in size and shape, marked central pallor, polychromasia, and no nucleated red blood cells. The blood sugar was 100 mg. per hundred cubic centimeters of blood; blood urea 22 mg. per hundred cubic centimeters of blood, and blood urea nitrogen 10.27 per hundred cubic centimeters of blood. The urine showed no pathologic changes. The Wassermann and Kahn tests were negative.

Biopsy section submitted showed keratosis follicularis.

DISCUSSION

DR. PUSEY: May I express my admiration of a clinic that can produce three cases of Darier's disease and three or four cases of Kaposi's sarcoma at the same meeting?

CASE FOR DIAGNOSIS. Presented by DR. WAY and DR. AYRES.

The patient, a man, was first seen Dec. 23, 1928, at which time he had an eruption with lesions scattered over the trunk and thighs. He stated that the condition began about five weeks previously with a small sized nodule, containing a thick, necrotic pus, on the side of the hip. The lesion spread rather rapidly in spite of local applications and five or six doses of an unknown amount of roentgen therapy. He was given potassium iodide orally, and after taking this for about ten days, he developed a profuse papulopustular rash, suggesting iodide rash. At this time the ulcer on the hip was the size of a child's palm, the patient felt bad and had a temperature of 101 F., or more. Numerous cultures from the lesions and the blood were negative, except that one culture (made before the patient was seen by the presenters) showed an unidentified yeast in combination with bacterial contamination. Dr. Roy Hammack found double contoured, yeast-like cells in one smear, but they could not be confirmed.

A biopsy specimen showed chronic inflammation of the tissue, but was not specific of any definite condition. Three Wassermann tests, one a provocative, were negative. The spinal fluid was reported negative when examined two years previously.

Many of the lesions which appeared to be iodide pustules developed into true ulcerations similar to but smaller than the original lesions; others dried up and disappeared.

The patient was put on colloidal copper intramuscularly, neoarsphenamine intravenously, and generalized exposure to the quartz light locally. Nine weeks later the lesions had entirely healed. He had received, in all, nine doses of neoarsphenamine and ten doses of copper. Two months later when he reported for observation the condition remained well.

The patient had had six or seven similar ulcerated lesions over a period of two years, commonly on the trunk, and never more than one or two at a time, the largest being about the size of a silver dollar. He had usually been cured by surgical and antiseptic treatment. On June 26, 1929, a new lesion appeared on the right hip which presented the same characteristics as the previous ones.

Smears from the blood and the lesion were negative for the Donovan-Leischmann bodies. Cultures showed a pure *Staphylococcus aureus,* while those made on Sabouraud's mediums showed an unidentified fungus.

SARCOID (?). Presented by DR. ALDERSON and DR. WAY.

J. C., aged 44, a Greek barber, came for treatment of a skin condition on April 10, 1929. He had been in the United States for twenty-three years. He stated that the first area of discoloration appeared on the lower left eyelid about eighteen months before and was soon followed by areas on the feet and then on the hands. The family history contained nothing of importance; there was no record of any skin disease in any members of the family. The patient gave a history of a chancre twenty-two years ago for which he received intramuscular injections at that time. He had recently received twelve injections of neoarsphenamine and from twelve to twenty injections of bismuth, the last in February, 1929. He had had a neisserian infection twenty-four years ago.

Physical examination revealed nothing of importance except many carious teeth, injected and hypertrophic tonsils and some sonorous râles through the chest.

The skin lesions were located on the dorsum of the hands and wrists, the toes and the soles. The lesions were elevated, somewhat indurated, purplish red and as

a rule confluent. There was complete anesthesia; the biopsy from hand and foot lesions produced no pain.

Laboratory observations: A Wassermann test on April 20 gave a negative reaction. Roentgenograms of the sinuses revealed thickening of the mucous membrane of the maxillary, sphenoid and ethmoid sinuses. On April 26 seven smears of serum from a vesicle produced by carbon dioxide snow were negative for Hansen's bacillus, as were smears from the postnasal secretion. On May 3 the Wassermann reaction was again negative. Examination of the blood May 6 showed: erythrocytes, 5,060,000; hemoglobin, 93 per cent (Sahli); color index, 0.91. Differential count revealed: polymorphonuclears, 64 per cent; lymphocytes, 31 per cent, and eosinophils, 5 per cent.

Histopathology (Dr. Way).—The epidermis shows thickening of the stratum corneum; many of the basal epidermal cells contain pigment in increased amounts. Otherwise there is little variation from the normal. The pathology of the corium suggests a possible toxic origin. The infiltration is more diffuse in the upper corium and more sharply demarcated or circumscribed in the deeper layers. The infiltrating cells, composed of lymphocytes, epithelioid cells and fibroblasts, occur largely in the vicinity of the vessels, and show varying degrees of endarteritis, but evidence of caseation is lacking. No tubercle bacilli, lepra bacilli or giant cells are found.

The patient was placed on treatment with gold sodium thiosulphate and had received six injections, the first three consisted of 0.05 mg. each, the fourth of 0.10 mg., the fifth of 0.15, and the sixth (on June 13) of 0.25 mg.

DISCUSSION

DR. STUART C. WAY: The appearance of this case when the patient was first seen suggested leprosy, but we could not find the Hansen bacillus. Sections suggested sarcoid, possibly of the Spiegler-Fendt (?) type. The condition is clearing up rapidly under treatment with gold sodium thiosulphate. When first seen the lesions were almost twice the size of those today and somewhat elevated.

DR. FINNERUD: I thought that from the appearance of the lesion, but chiefly from the histologic section, it was Kaposi's sarcoma. The slide showed what histologically is one of the three characteristic pictures of that disorder. My clinical impression was strengthened by the noting of a verrucous aspect to the skin of the dorsum of the toes at their sides, a feature which seems to me to be almost a constant observation in this disorder when there is involvement of the lower extremities.

PROFESSOR JADASSOHN: I am not sure whether Dr. Way said that in the beginning the picture was that of lupus pernio. I believe it could be either a Kaposi sarcoma or a lupus pernio, and a study of a biopsy seems to be necessary for diagnosis. The sarcoid of Boeck and lupus pernio are so frequently negative to tuberculin that this fact would make this diagnosis more probable especially if there are the well known infiltrations which are found in the lungs in the sarcoid group.

FIBROANGIOMA (MULTIPLE). Presented by DR. NORMAN EPSTEIN.

J. J. W. M., aged 12, presented four nodules in the skin of the right little finger and the ulnar side of the right hand, arranged in a linear manner. The largest was situated over the middle interphalangeal joint and was more superficial than the others. They were bluish-red and nontender.

The first lesion appeared on the right little finger six years before presentation, several months after an injury to the part, and recurred after excision. The other lesions had developed within the last three years.

Physical examination showed no pathologic changes, except for the skin lesions, and a roentgenogram of the right hand revealed no bony changes.

Biopsy showed an angiomatous structure, with increase in the connective tissue stroma.

COCCIDIOIDAL GRANULOMA. Presented by DR. CHIPMAN and DR. TEMPLETON.

This patient was the second one reported in the paper by this title to be presented at the meeting of the American Dermatological Association of 1929.

The patient had never been in the San Joaquin Valley, but the onset of his trouble was in August, 1925, five months after he began working in a cotton mill which received its cotton from that district.

The first manifestation of the disease was involvement of the glands of the neck, the skin and bones not becoming involved until a year later. On May 1, 1929, he was in the hospital in a critical condition. The cutaneous lesions were active, and the sinuses over the involved bones were discharging large quantities

Photographs of lesions when active.

of pus. He was placed on colloidal copper intramuscularly, and a vaccine consisting of a suspension of killed coccidioides immitis. The improvement had been striking. There was complete healing of the sinuses and marked betterment in the cutaneous lesions.

A CASE FOR DIAGNOSIS. Presented by DR. AYRES, JR.

This patient was first seen on June 7, 1929, because of a lesion on the right ankle which had been present for nine months. He stated that it began as a small, dry, scaly spot, the size of a silver quarter, which gradually enlarged. He had received various local applications and quartz light therapy, and eleven teeth had been extracted following examination by the roentgen ray. He stated that twenty years before presentation his right leg and ankle were run over by an ice wagon, and that he had had arthritis in the ankle, wrist and several other joints for many years. Until about three months ago he had considerable gas and bloating of the stomach.

When first seen the affected area was covered with numerous purulent, thick crusts. Under antiseptic wet dressings, bland antiseptic ointments and three fractional doses of roentgen ray the condition had improved markedly, although there had been no obvious diminution in the size of the nodules.

Direct smears and cultures on Sabouraud's medium were negative except for bacteria.

Histopathology (Dr. E. M. Hall).—Paraffin sections show hypertrophy of epidermis; long, finger-like processes of stratum mucosa extend down between the connective tissue papillae. The basement membrane is everywhere intact. Stratum corneum is irregular in thickness or missing. Some vacuolation of cells is present in superficial parts of stratum mucosa.

Giemsa stains show under oil fine cobweb-like filaments with many sporelike forms apparently in the filaments about the cells in the derma. These filaments stain blue and do not appear to be fibrin. The small sporelike forms also stain blue and are slightly smaller than an ordinary coccus. These filaments and sporelike forms suggest one of the higher bacteria, such as the streptothrix.

A few polymorphonuclear leukocytes are present and a moderate number of eosinophils.

DISCUSSION

Dr. MacKee: I think this is a breaking down of roentgen ray skin; chronic radiodermatitis, with telangiectasia, atrophy, sclerosis and ulceration. I advise excision followed by a graft on a tubular flap.

Dr. Ayres: The patient says he has never had roentgenotherapy, except for the three treatments of 0.25 skin unit each which I have given, which have not changed the appearance of the lesion.

Dermatitis Herpetiformis. Presented by the University of California.

E. D., white, aged 50, was first seen in the clinic in January, 1929, when he had a disseminated papular eruption with severe pruritus. At that time there were numerous excoriated papules symmetrically distributed over the legs below the knees, the forearms, back and shoulders. These lesions had been recurring for four years. No bullae were present.

There was a history of a neisserian infection in 1907, and of a possible primary sore in 1909; no therapy was given. In 1916 he was told that he had pulmonary tuberculosis.

The laboratory observations, including the blood chemistry, were negative. Biopsy revealed results that were consistent with the diagnosis.

The patient had been improving slowly with light therapy, diet and local medication.

Actinomycosis (Cured). Presented by the University of California.

W. F., a white man, aged 19, had lived in California all his life. He had no contact with cattle but stated that he occasionally chewed straws. In November, 1926, a swelling developed over the region of the left mandible. An impacted left lower third molar was extracted, and on incision pus was obtained which was positive for *Actinomyces bovis*. Potassium iodide was administered by mouth but was not tolerated well. Repeated abscesses in the skin developed which were in turn surgically treated.

In July, 1927, he reported to the Skin Clinic of the University of California with several abscesses following along the border of the left mandible. *Actinomyces bovis* were obtained in smear and culture.

Treatment had consisted of sodium iodide intravenously, thirty injections of 2 Gm. each, without marked improvement. He was then given four intravenous injections of typhoid, paratyphoid A and B, 75,000,000, 100,000,000, 125,000,000 and 150,000,000 organisms, respectively, followed by rapid improvement. In January, 1928, the patient was apparently well.

Coccidioides. Presented by the University of California.

D. H., a white man, aged 33, was first seen in the clinic in May, 1929, because of stiffness of the left knee of eight months' duration. He had lived in Ireland

until he was 30, and then went to the San Joaquin Valley to work in the oil fields. His health had always been good, but about two months after beginning this work he developed pleurisy and was in the hospital for three weeks. Following this he began having night sweats, loss of weight and weakness. He also developed severe pain in the lumbar region, and a lesion on the back of his left hand. A smear from this lesion was diagnosed as *Coccidioides*. In November, 1926, an operation was performed on his back and on his hand.

In January, 1928, a skiagram of the chest showed evidences of an old infectious process in the right base, now healed. Roentgenograms of the left hand showed that the left metacarpal was a mere shell in its outer half, an old osteomyelitis. The appearance of the lumbosacral spine suggested an old infectious process.

In May, 1929, physical examination revealed impaired resonance in the lower part of the right side of the chest, with râles.

The laboratory observations were negative except that on microscopic examination of a smear of pus taken from the sacral abscess the double contoured bodies of coccidioides were found.

The patient had received numerous intramuscular injections of colloidal copper during 1927 and 1928. On May 30, 1929, 0.1 cc. of coccidioides vaccine was administered intradermally, the wheal fading in forty-eight hours. On June 3, 0.1 cc. of vaccine was given subcutaneously, with slight reaction within twenty-four hours, erythema and swelling of the lesion on the leg. On June 5, 0.1 cc. of vaccine was given subcutaneously.

DERMATITIS (SEBORRHEIC) (?). Presented by the UNIVERSITY OF CALIFORNIA.

KELOIDS (IDIOPATHIC). Presented by the UNIVERSITY OF CALIFORNIA.

COLLOID DEGENERATION OF SKIN. LUPUS ERYTHEMATOSUS. Presented by DRS. MORROW, MILLER and TAUSSIG.

Approximately twelve years before presentation the patient noted the development of translucent papules on the dorsal surfaces of his hands, appearing coincidentally with an extensive lupus erythematosus of the face. The patient had been under their care off and on for six years for treatment of lupus erythematosus, and since October, 1928, had received fourteen injections of gold sodium thiosulphate, with considerable benefit to the remaining active lesions of this disorder. During this time there had also been a definite decrease in the area presenting colloid degeneration.

Biopsy showed colloid degeneration of the skin.

DISCUSSION

DR. MILLER: This patient was presented because of the areas of colloid degeneration on the hands which developed at the same time as the lupus erythematosus on the face. The condition on the hands is involuting under gold and sodium thiosulphate therapy about as rapidly as the lupus erythematosus is on the face.

CONDYLOMATA LATA ALOPECIA (SYPHILITIC). Presented by DRS. ALDERSON and WAY.

PARAFFINOMA. Presented by the UNIVERSITY OF CALIFORNIA.

LEUKODERMA. Presented by DR. H. C. L. LINDSAY.

KERATOSES (ARSENICAL). Presented by the UNIVERSITY OF CALIFORNIA.

PHILADELPHIA DERMATOLOGICAL SOCIETY

CARROLL S. WRIGHT, M.D., *Secretary*

Nov. 1, 1929

ABRAM STRAUSS, M.D., *Presiding*

SEBORRHEIC DERMATITIS IN A SERIES OF CASES OF POSTEPIDEMIC ENCEPHALITIS. Presented by DR. WEIDMAN.

Three men were exhibited from the wards of the Philadelphia General Hospital. All had greasy faces. In addition, one had a patch of thick seborrheic crusting of the scalp; the second showed numerous papules, presternal and extending upward onto the shoulders; the third showed a dozen or more superficial scaly, greasy, hyperpigmented patches over the sternum which extended laterally even into one axilla. *Microsporon furfur* and *Pityrosporum ovale* were present in great numbers in scrapings from the latter case, but only *Pityrosporum ovale* was found in the other two.

The three men were the most representative of the patients with seborrheic dermatitis observed in a survey of all the cases of postepidemic encephalitis in the hospital (twenty-seven available). Out of these, ten or 35 per cent, showed at least a seborrhea, and in addition, a diffuse patchy type of dermatitis that was typically seborrheic but for the most part papular, that is, acneiform. The most convincingly seborrheic types were those in which the distribution was presternal and interscapular; this was seen in the 35 per cent already mentioned. The probability is that at the bottom of the dermatosis there is a disturbance of the sympathetic system. Epidemic encephalitis has its seat in the basal ganglions, but as far as neurologists know at present, they cannot establish any certain connection with the sympathetic system. All of the neurologists, though, are agreed that sweating is a conspicuous symptom in these cases, and that the face is consistently greasy. The probability, Dr. Weidman thought, was that the order of the process was the same with the dermatosis as in regard to the control of the musculature, which, of course, was responsible for the forced movements of this disease; that is, there was a release of inhibition so that the tonic muscles were allowed unduly free play. Similarly, in regard to the sympathetic system, the prohibiting factors were released and we had this undue sebaceous secretion. That, of course, only took us through one part of the problem, that is, the question of the excessive secretion of sebaceous material. In connection with the tinea versicolor which was associated with the seborrhea in case 3, the presentor recalled a case of erythrasma in which he had found both *Microsporon furfur* and *Microsporon minutissimum* in the lesions of the chest and the axilla. It is quite possible from that that these two organisms, as well as *Pityrosporum ovale* are favored by the presence of some preexistent infection or some preexistent abnormal state like seborrhea. The presentor expressed the belief that the mechanism in these cases was first an excessive greasiness of the face and then parts of the body, and that thereafter there was superimposed on the condition, the infection with *Microsporon furfur*, and the reproduction of the associated inflammatory features.

The condition was also found in women with epidemic encephalitis, but less highly developed. In one woman there were patches under both breasts much more infiltrated than anything these patients show.

Patients do not show the skin disease in the early stages of the disease. The three men mentioned here were in the hospital, bedridden, for from three to four years. The dermatitis appeared only in the later stage of the disease and in those cases in which the forced movements were most marked. Once again, these cases illustrate the close connection between internal medical states and the surface.

DISCUSSION

DR. SCHAMBERG: I have been very much interested in this presentation of Dr. Weidman's, and I must say that it demonstrates his ever present mental alertness in deducing relationships of cutaneous diseases to systemic manifestations. I think that one must exercise a certain mental reservation in these cases and not necessarily deduce that the seborrheic dermatitis exists in essential relationship to the preceding epidemic encephalitis. It would require, I think, a very large series of cases in order to form a definite deduction of that connection because after all, seborrheic dermatitis is a relatively common disease. We see it almost every day in practice, and we must realize that we may be misled through certain coincidences. We may find a certain disease in a group of persons, and yet the disease may have no essential relationship to the systemic condition from which the patients are or have been suffering. Therefore, I would not want to come to any definite decision that these cases represent more than a coincidence. I think the matter deserves careful study and search among larger groups of subjects with encephalitis to see whether there is an increased incidence of seborrheic dermatitis among them.

There is a number of very common skin diseases, for instance, acne; when I examined about 600 students of Jefferson Medical College for demobilization, I was astonished at the extremely large incidence of acne among young men. I formed the impression later that 75 per cent of the men had some acne on the face, shoulders or back, and if they had served in the army and we had made a numerical count we might have come to the decision that army life predisposed to acne. While I think this is worthy of further study, I feel that one must reserve one's opinion as to the definite relationship.

DR. CORSON: I was wondering if the helplessness of these patients would not have something to do with the aggravation of the disease; whether their inability to care for themselves would not make it more apparent. I think it would be interesting to observe some of the other patients with nervous diseases at the Philadelphia Hospital who are relatively as helpless as these persons and see whether they show dermatosis which might result from improper hygiene.

DR. WEIDMAN: These points are, of course, very properly taken, but I thought that it was the high proportion of seborrheic lesions, the incidence, that was certainly a very definite lead. As a matter of fact, twenty-seven cases of post-epidemic encephalitis constitutes a large series. I doubt if there is any other place in the United States where so many cases are gathered together in one place, and the fact that ten of those showed definite involvement of the seborrheic distribution must mean something significant. In those ten I did not include simply greasy face and pityriasis, I only included those cases in which there were presternal and interscapular lesions as well as the scalp lesions. I made it a point to inquire into the hygiene of the nervous wards; the patients are bathed twice a week. The matter of the presence of seborrhea in other nervous patients has also been covered; in order to cover the contingency that possibly it might be simply excessive muscular effort or exercise that was the determinant (perhaps only nervous, perhaps muscular, perhaps both), I examined six cases of true Parkinson's disease (these late cases of encephalitis are sometimes designated "parkinsonian" because their muscular movements simulate those of paralysis agitans); none of the six showed the seborrheic condition that seemed to be so common in these cases of sleeping sickness. Of course, there is little that is final in dermatology, certainly not in the first presentation, but I think this is a very strong lead.

MYCOSIS FUNGOIDES. Presented by DR. WEIDMAN.

S. H. W., aged 59, gave a history of having been employed in a place where strong chemicals were used—ammonia, vitriol, lye, etc. He stated that the condition (a generalized erythrodermia) began seven years before presentation. Itching was marked. When I first saw him I tried to see if I could eliminate

the possibility of Hodgkin's disease or lymphatic leukemia. I have not been able to do that satisfactorily. The first red blood cell count was 2,600,000, rising slowly to 4,070,000, and, of course, the hemoglobin has similarly risen. On admission, the white blood cell count was 9,000; later it was 7,000, then 8,000, and at present it is 9,700. The ratio of polymorphonuclears had always been within normal limits. A roentgenogram of the chest showed evidence of an enlargement of the lymph nodes. Biopsy was performed, but the picture was only suggestive of mycosis fungoides.

I always hesitate to make a positive diagnosis of this disease in the absence of a full series of changes in the skin. The closest I can come to diagnosis in this case is that it is a premycotic condition. While the tongue was swollen and red, and there was marked adenopathy, I think these symptoms are among the least dependable in the diagnosis of these leukemic states. In the Philadelphia General Hospital we frequently encounter occupational dermatosis, chrysorobin dermatitis, etc., and in these also I have noticed that the lymph nodes are consistently enlarged and that the tongue is large, swollen and red.

DISCUSSION

DR. SIDLICK: I cannot accept a diagnosis of mycosis fungoides. It is not usual in a premycotic stage to find the skin to be uniformly involved as in the present case, and furthermore the itching that a patient with mycosis fungoides would have would be severe and the patient would be unable to sleep. Here, from a clinical observation of the patient and also from his statement, the degree of itching is apparently very mild.

DR. CORSON: I should call the condition chronic scaly erythrodermia. In seven years it should show more change. It may, of course, be premycotic.

DR. WRIGHT: I think that this case well illustrates the difficulty of making a diagnosis on purely clinical grounds. This patient has the appearance of a man I studied at Ann Arbor, in 1921; we were definitely able to prove the condition to be leukemia cutis, and it was later reported as such by Dr. Keim. However, throughout the course of the disease, the patient ran a leukocytosis of 25,000 or more, and he had a definite lymphocytosis. From the appearance of the skin alone we could not definitely say that the case presented here is premycosis fungoides.

DR. SCHAMBERG: I have seen a number of cases of this character in the course of years. They are very difficult to diagnose. Some of them are cases which one would designate as chronic scaly erythrodermias; others are cases of leukemia cutis or Hodgkin's disease; still others have been due to tuberculosis, and then a group of them have been cases of mycosis fungoides. One can never positively exclude mycosis fungoides because the eruption may exist for ten years before the classic tumor stage develops. I think that one is not justified here in definitely pronouncing a diagnosis beyond a chronic exfoliative erythrodermia; of course, suggesting that some day the patient might develop evidences of mycosis fungoides, particularly if the microscopic sections of the skin do not show the initial evidences of the disease. These constitute a very tragic type of condition because they are among the most refractory conditions we encounter. They start from various diseases, from dermatitis herpetiformis, pemphigus, eczema and psoriasis, and develop into this condition. I would not want to make an absolute diagnosis except to make a diagnosis of the symptoms as they present themselves.

EXTENSIVE LUPUS ERYTHEMATOSUS AND LUPUS VULGARIS. Presented by DR. WEIDMAN.

I saw this patient in the wards of the Philadelphia General Hospital two months ago and the first thing that struck my attention was the condition in the external ear. This, together with the atrophic scarrings on the scalp, at once satisfied me that this was what had been diagnosed by my predecessor as a disseminated lupus. But three or four weeks later I found nodules in the margins

of certain patches on the face, translucent, apple jelly-like nodules. Sections showed classic tuberculosis with caseation. The patient had pulmonary tuberculosis; the roentgenologist reported an old bilateral fibrocaseous process. I do not think there is any doubt at all about the lupus erythematosus phase. On the tips of the ear there were as classic horny plugs as one could want, and also on the shins. Patches on the forearm were so atrophic that one could see the veins, as in acrodermatitis chronica atrophicans. A thing that had not yet been done, was to find out whether the tuberculosis bacillus was present in the nodules on the skin.

DISCUSSION

DR. KAHN: This patient has been in the hospital since June or July. He was covered with dry white scales and at the time of admittance there was no atrophy. At first we thought possibly we were dealing with a syphilitic condition, but the Wassermann reaction was negative. A diagnosis of tuberculosis cutis was then made.

DR. SCHAMBERG: The case presented by Dr. Weidman is one of very great interest. I think we must recognize today that there are more types of tuberculosis of the skin than used to be stated in the old textbooks on dermatology, and furthermore, that one type may run into another. I quite agree with Dr. Weidman that this man has a tuberculosis of the skin presenting many lesions which might be classified as lupus vulgaris and, on the other hand, he presents lesions which, if seen alone, would be regarded as lupus erythematosus; but just as syphilis presents great varieties of cutaneous manifestations, so does tuberculosis. I think we are inclined to be too closely bound by medical tradition, feeling that the symptoms of lupus vulgaris are such, those of scrofuloderma such, etc., and fail to realize they are all manifestations of the same parasitic invasion. It is quite possible here that we have tuberculosis of the skin which presents varying manifestations. Dr. Weidman has shown several other cases in the past few years, one of generalized nodular tuberculous eruption of the skin in a woman who ultimately died of tuberculosis, a case that looked like syphilis in the beginning. Such cases have no special classification in dermatologic literature. They are not lupus vulgaris in the true sense nor any of the other types of tuberculosis, so we find these variant types and variant conjunctions of clinical manifestation. I think Dr. Weidman is justified in calling this a case of lupus vulgaris with lupus erythematosus; the only reserve thought in my mind is that these atrophic areas may be atrophic areas of superficial actual tuberculosis of the skin, bacillary in character, and not be what we ordinarily call lupus erythematosus. These lesions are in many cases very superficial; some of the nodules are extremely small, and one may have a very fine nodular infiltration which after involution leaves the atrophic areas looking like the classic type of lupus erythematosus. It is a very unusual and instructive case.

DR. GREENBAUM: I agree substantially with what Dr. Schamberg has said, but there is one point which ought to be brought out, the relation of this skin disease to tuberculosis. I recall a year spent in the service at Blockley. I do not believe I saw one patient with cutaneous tuberculosis, so that the relationship between this patient's skin and his lungs is not obvious in respect to other patients who have lupus vulgaris and lupus erythematosus, and no pulmonary tuberculosis.

DR. SCHAMBERG: It is true that if one goes through the tuberculosis sanitoria of this state one may find no case of lupus vulgaris, which merely means that lupus vulgaris is rare among tuberculous patients. But systemic tuberculosis is so common among patients with lupus vulgaris, that it is almost universal.

EXFOLIATIVE DERMATITIS FOLLOWING OCCUPATIONAL DERMATOSIS. Presented by DR. WEIDMAN.

C. S., a man, aged 42, exhibited a generalized, diffuse erythrodermia with thickening, together with superficial branny exfoliation and numerous excoriations. In addition, there were numerous slightly elevated nodules over the arms and

elsewhere. The palms and soles were tremendously hyperkeratotic; on admission, the accumulations were fully a centimeter thick. The hair of the eyebrows was thin from rubbing; the scalp hair was thin and the scalp itself covered with excessive fine branny desquamation. The tongue was thick, beefy red, and coated. There was general adenopathy.

According to the patient he had had exfoliations at intervals for thirteen years, disappearing in winter and returning in summer. He had been liable to sore throat; his tonsils were removed eight weeks before presentation. He had lost 30 pounds (13.6 Kg.) since the previous June but regained some of the weight while in the hospital. He had worked in a flour mill.

A particular incident in this case was the development, about three weeks after he was admitted to the hospital, of a varioliform eruption which appeared particularly over the arms and the upper part of the chest, but also on the legs and face. There were no constitutional symptoms. One of the officers in the hospital thought it might be smallpox, but it was not definite enough to warrant quarantine. I felt that it might be one of the expressions of a leukemia, a leukemid. I have seen a similar varioliform dermatosis in a patient who subsequently died; in addition to this, there was a marked angina with extreme granulocytosis.

In this patient we had to contend with the question of autoinoculation from vaccination, but the inoculation did not take at the site of the primary inoculation. Now that the varioliform lesions have disappeared we see no pittings; the condition was certainly neither variola nor vaccina. (Four weeks after presentation, some very superficial pittings were discernible in the upper part of the arm, but not elsewhere.)

DR. GREENBAUM: I saw this patient eight or nine months ago. He was in the hospital two weeks, and then we were forced to discharge him due to lack of room. At that time I made the diagnosis that Dr. Weidman has made of generalized eczema of occupational origin. He is much better than he was; the skin of the face and arms was definitely swollen, oozing, red and crusted.

A CASE FOR DIAGNOSIS. Presented by DR. GEORGE WOOD.

Mrs. E. D., aged 35, was admitted to the Graduate Hospital on Sept. 26, 1929. Her present condition began in March, 1929, with nasal discharge and had been gradually getting worse. About three weeks before coming to Philadelphia, a swelling of the lip was first noticed, which the patient thought followed her first injection of arsphenamine. On admission to the hospital there was inflammatory infiltration of the upper lip and around both nostrils excoriation of the vestibules and some general swelling of the nose especially toward the tip. The interior of the front of the nose was filled with foul smelling sloughing material which, on being pulled out, left a bleeding granulation area. The bone was bare over the front part of the nose but a good view of the interior of the nose could not be obtained because of extreme tenderness. The odor was characteristic of atrophic rhinitis. The cartilage in the center had been destroyed. Roentgen examination showed no involvement of the accessory sinus.

Results from a Wassermann test from the State Laboratory on August 29 were negative. The patient had been taking corrosive mercuric chloride and sodium iodide for one month and had had two intravenous doses of 0.06 Gm. of sulpharsphenamine and two doses of 0.60 Gm. of neoarsphenamine previous to her admission to the hospital. She was suffering with almost constant aching pain across the bridge of the nose and in the face.

In consultation, Dr. Greenbaum suggested smears for diphtheria and spirilla and fusiform bacillus, but he believed the condition to be a gumma and advised 0.45 Gm. of neoarsphenamine and 0.1 Gm. of bismuth twice a week for ten doses.

The blood count showed: red cells, 3,800,000; white cells, 14,000; hemoglobin, 68 per cent; lymphocytes, 20 per cent and polymorphonuclears, 80 per cent.

Smears from the nose on September 30 showed: Staphylococcus, B. subtilis and diphtheroid organisms. There were no tubercle bacilli. Guinea-pigs that

were inoculated died of streptococcic abscess and septicemia. On Sept. 30, 1929, the complement-fixation test for glanders was negative. On October 16, with the patient under ether, the nasal fossae were examined, and a piece of tissue was removed from the left side of the floor of the nose for biopsy. The biopsy report was diffuse fibrous tissue and granulation tissue. A diagnosis of chronic inflammatory lesion, not syphilitic, was made. October 23, scrapings did not show actinomycosis on the smear.

The treatment given has been chiefly the use of various antiseptics in the nose: carbolized glycerin, tincture of iodine; the lesion was twice curetted out under anesthetic.

DISCUSSION

DR. SCHAMBERG: This woman presents marked rigidity and infiltration of the tip and alae of the nose, the same being highly inflammatory. One naturally thinks of rhinoscleroma, but one does not see this highly inflammatory redness in this condition. Rhinoscleroma often presents the color of the normal skin and a degree of hardness which is almost stony. Then, too, it is excessively rare in the United States. In Hungary and in surrounding countries, it occurs frequently. In thirty-five years I have never seen a case in my clinic. So that, while it presents more resemblance to that than to any other condition, it is doubtful whether it is rhinoscleroma.

I do not believe that the condition is syphilitic. It is very unusual to find this extreme rigidity in syphilis, and the serologic tests and results of treatment have been negative. I do not believe that it is tuberculosis. The question is, what might it be? It is still possible that we have a sclerosis of the wings and tip of the nose with involvement of the vestibule, which may be due to some hitherto unknown organism, and I think it is along this line that further search must be made. I think that more animal inoculations should be made with smears and scrapings from the parts, and it seems to me the question of diagnosis lies between a sclerosis of the nose due to infection of some hitherto undescribed or undiscovered organism, or an aberrant type of rhinoscleroma.

I believe that the best line of treatment, apart from keeping the parts clean, is the use of the roentgen rays, which also is good therapy in cases of rhinoscleroma. Of course, every effort should be made, from a scientific standpoint, to elucidate the cause of the condition.

DR. WEIDMAN: I think that the presence here of Dr. Wood guarantees that the case has been already gone into as thoroughly as can be expected from the clinical angle. I think, as Dr. Schamberg said, that further hope lies in the laboratory examinations. I was not quite clear as to what the biopsy had revealed. It often happens, when there is ulceration like this, that biopsies are not taken deep enough; only the surface granulation tissue is submitted to the pathologist. Of course, in a place like this we are handicapped, but I think that there is still hope in a deeply taken biopsy. From the standpoint of tuberculosis, the antiformin technic will kill a lot of contaminating bacteria, and thereafter the inoculation of guinea-pigs will often enable one to recognize a case of tuberculosis that otherwise would be overlooked.

SYPHILITIC DACTYLITIS. Presented by DR. SIDLICK.

A woman, aged 40, had the condition for two years. At first the palm showed a vivid, uniform infiltration and later a number of fingers of the hand were involved. In addition, the patient presented peculiar pain and swelling of the index, middle and little fingers of the right hand and the little finger on the left hand. This condition had improved considerably within the ten days following the administration of iodine. The Wassermann and Kahn reactions were strongly positive.

HYDROA PUERORUM. Presented by DR. GREENBAUM.

A boy, aged 5, was seen for the first time on August 28. Two days previously the mother noticed a blister near the site of an old burn, and new blisters formed

rapidly until most of the body and face and scalp were covered with large bullous areas, with a tendency to grouping. They were purulent in nature. The boy's blood count was as follows: eosinophils, 15 per cent; leukocytes, 15,700; hemoglobin, 58 per cent. A good many of the lesions have disappeared.

DISCUSSION

DR. WRIGHT: I presented this case in clinic the other day with a diagnosis of dermatitis herpetiformis, so in order that there may be no confusion in the minds of students present, I think Dr. Greenbaum really is just giving the condition a name to make it more difficult and the dermatosis really is a dermatitis herpetiformis. I have seen a number of these cases in children, and as a therapeutic measure, I might say that they usually respond very readily to injections of sodium arsenite and perhaps locally, the use of mild antipruritic lotions.

DR. WEIDMAN: What is the connection between this and the scar?

DR. GREENBAUM: The burn occurred almost a year before the eruption appeared, and I doubt if there is any relation.

CREEPING ERUPTION. Presented by DR. CORSON.

R. D. M., aged 58, had the eruption for about five months. There was no special difficulty about the diagnosis of creeping eruption or larva migrans, but this case has been unusually resistant to treatment. He has had various treatments at different places. So far, all the larvae have not been destroyed. There are four active foci at the present time. He states that at the University Hospital they used a freezing method with carbon dioxide snow and ethyl. We have mainly employed freezing with ethyl chloride.

DISCUSSION

DR. GILMAN: We saw this man at the University Hospital two months ago. We treated him with ethyl chloride, for at the time we were unable to use carbon dioxide snow. We had a fair amount of success but some lesions advanced in spite of treatment, and in desperation we used electrofulguration. At a subsequent visit we thought we had destroyed most of the lesions. The patient presents about the same appearance as he did at the University Hospital, with six or eight active lesions.

DR. WRIGHT: For those particularly interested in this subject, I would refer them to the published studies of Dr. Kirby-Smith.

MALIGNANT PAPULOMA. Presented by DR. SCHILDKRAUT.

A man, aged 32, had at the time of presentation a fungating growth about the size of a fist on his left shoulder which has recurred three times in the past eight years. He gave a history of noticing a little wart eight years before presentation, from which this lesion developed. In February, 1928, he had it excised. It recurred, and in November of the same year it was excised and electrocoagulated followed by roentgen-ray treatment. A low grade malignancy was reported by the pathologist.

DISCUSSION

DR. SIDLICK: I think that the condition is dermatitis vegetans, and if removed by the knife it will merely grow again.

DR. GREENBAUM: Has a biopsy been made?

DR. SCHILDKRAUT: The sections show marked hyperkeratosis. It gives me the general impression of an epithelioma of low grade malignancy.

DR. WEIDMAN: The sections were not good enough for diagnosis. The patient stated that the disease began as an acrochordon. I think it is a neoplasm but a very slowly growing one as malignant tumors go, in spite of what the patient says. He stated that it grew rapidly in the past three years, that he was operated

on twice, lesions were excised once and the second time electrocoagulated, and that this growth is only of one year's duration, which is fairly fast. I might add that he is not emaciated. It is not a bloody lesion like the free-growing sarcomas. All of these items support the idea that it is one of the less malignant affairs like endotheliomas.

ICHTHYOSIFORM DERMATITIS SUCCEEDING ON EXFOLIATIVE DERMATITIS. Presented by DR. WEIDMAN.

Bertha H., colored, aged 46, was studied five or six years ago in the Polyclinic Hospital and her case was undoubtedly diagnosed as pemphigus. She received sodium cacodylate and was referred to the Philadelphia General Hospital. On admission there, she developed exfoliative dermatitis of the Wilson-Brocq type, the scales at first being large and flaky. During the six years that she has been treated there, the type of skin has changed. It has taken on a Morocco leather, shagreen appearance in parts and the flexures of the elbow have developed definite ridges, almost ichthyotic. At the same time the skin has become hyperpigmented in various places and for a moment, occurring in the axillae and in view of that fine pebbly quality, the suspicion that it might be related to acanthosis nigricans arose. That can be dismissed readily on more careful analysis, which need not be detailed. The reason I have presented this case is to show the members what may be the progress of cases from time to time and the different kinds of change which the skin can show in connection with one of these chronic erythrodermias.

DISCUSSION

DR. SCHAMBERG: This case is of interest because it began as a classic pemphigus. I have an excellent photograph of the original condition which showed large blebs all over the extremities and body. We recovered from her blood a rather curious organism, a lanceolate streptococcus-like organism from which a vaccine was made. Under the administration of that, the blebs dried up; after that the patient developed a condition somewhat similar to what she has now, but with slight exudation beneath the peripheral skin resembling a pemphigus foliaceus. In the course of time the glands have enlarged and the skin has become coarser and drier. The point of interest is that one can get almost the same terminal result following a number of diverse dermatoses. We had together at one time, a chronic exfoliative dermatitis following psoriasis, dermatitis herpetiformis and psoriasis.

THE FOUR CITIES DERMATOLOGICAL SOCIETY (CINCINNATI, CLEVELAND, DETROIT AND PITTSBURGH DERMATOLOGICAL SOCIETIES)

LOUIS WILLARD, M.D., *Secretary*

Regular Semi-Annual Meeting, Nov. 9, 1929

HOWARD T. PHILLIPS, M.D., *Presiding*

AMEBIASIS CUTIS (ULCERATIVE)? Presented by DR. CRAWFORD.

A negress, aged 55, complained of an ulceration about the anus four years before presentation. This gradually enlarged until each buttock was involved in an irregular ulceration 9 by 12 cm. with deep precipitate and serrated edges. The diagnosis at first was thought to be tuberculosis cutis (ulcerated), but *Ameba histolytica* was found in quantities in the stool, and scrapings of the border of the lesions showed many of the same organisms. The organisms have not been

found in the sections. The edges of the ulcer have been excised on four occasions, each time breaking down again. The left side was healed, but the right side presented a large open wound 17 by 14 cm. with granulating edges. Fifteen injections of neoarsphenamine and forty of emetine were of no benefit.

DISCUSSION

DR. ELLER: This case fits in clinically, but not entirely, with the picture described by Engman, because Engman's case gave a history of amebic dysentery at times.

DR. CRAWFORD: Amebae are still found in abundance in stools. The pathologist who previously made a diagnosis of carcinoma now favors a diagnosis of amebiasis cutis. I shall follow Dr. Highman's suggestion to apply neoarsphenamine locally.

LYMPHANGIOMA AND ELEPHANTIASIS. Presented by DR. HOLLANDER.

A man, aged 36, presented a great number of small, circumscribed tumors in the groin, coalescing into large tumor formation with an elephantiasis of the scrotum. The condition was of eighteen months' standing, progressively getting worse, with blockage in the deep lymphatics in the pelvis, the cause of which was undetermined.

DISCUSSION

DR. CRAWFORD: Elephantiasis is not a diagnosis, but only a condition. I think that this is a case of granuloma inguinale.

DR. LAVENDER: I agree with Dr. Crawford's diagnosis. Lesions like this do not improve under treatment with tartar emetic. In cases similar to this diphtheria antitoxin was given with improvement.

DR. COMBES: I think that this is a case of granuloma inguinale. There is a fear of giving too much tartar emetic. As high as 10 cc. of 1 per cent has been given every four days with no harmful effects and good results.

DR. RAUSCHKOLB: I have seen a series of cases of granuloma inguinale in the past year in colored people. Tartar emetic is as specific for granuloma inguinale as arsphenamine is for syphilis. Three patients who were being treated by tartar emetic died of miliary tuberculosis.

DR. HOLLANDER: The 4 plus Wassermann reaction became negative under antisyphilitic treatment but the nodules remained. Sections did not show Donovan bodies.

PSORIASIS LIMITED FOR TWO YEARS TO THE HANDS AND FEET. Presented by DR. WILLARD.

A white woman, aged 40, presented a scaling rash of the palms and fingers of three years' duration. Similar sharply marginated, rounder, paler areas had recently appeared on the feet, upper inner part of the thighs, axillae and scalp. Wassermann reactions of the blood had been repeatedly negative. The eruption had disappeared after six injections of neoarsphenamine, but had promptly returned. The same result had been obtained with a total dose of one unit of roentgen ray with prompt relapse. No improvement had followed the use of chrysarobin ointment. The patient was presented for counsel as to further treatment.

DISCUSSION

DR. HOLLANDER: I saw this case about two years ago and considered it a tineal infection. The presence of lesions on the legs and crural region now is suggestive of tineal lesions instead of psoriasis.

DR. HIGHMAN: The patient has tinea and the lesions mentioned by Dr. Hollander in the crural folds and also the lesions on the calves are tinea. The patient has a tricophytide with a psoriatic habitus. Some skins have a tendency to lichenification and some to psoriasiform lesions. It is uncertain whether the

patient has a tineal eruption resembling psoriasis or psoriasis with tinea on top. I believe that the patient has tinea of the psoriasiform type.

DR. SCHEER: I believe that this is a case of psoriasis and not tinea. I have seen such cases beginning in the crural region and extending. I cannot agree with the diagnosis of tinea and believe it to be a case of psoriasis in all locations.

DR. LAVENDER: I recall two cases like this with positive mycotic cultures, which after treatment by the roentgen ray and ointment closely resembled psoriasis. Perhaps the roentgen ray may be the cause of a transformed picture.

DR. FISHER: The picture on the hand is that of psoriasis.

DR. PARKHURST: The lesions on the scalp are psoriatic.

DR. RUBENSTEIN: The finger-nails show evidence of psoriasis.

DR. SCHEER: According to Dr. Heller, pitted nails do not necessarily mean psoriasis. Red, scaly macules underneath the nails are the only conclusive evidence of psoriasis of the nails.

DR. HIGHMAN: The lesions on the scalp suggest psoriasis, but the eruption may be a severe case of seborrhea. Psoriasis of the palms and soles is rare. If the palms are examined, closely macerated lesions are seen with vesicles underneath. No definite changes are seen in the toe-nails but a disturbance which might be psoriasis or tinea is seen.

DR. HOLLANDER: The patient has a few lesions developing rapidly which may be trichophytide according to Dr. Williams.

DR. WILLARD: The lesions on the calves and legs have developed recently since the patient's teeth were extracted.

A CASE FOR DIAGNOSIS. Presented by DR. GUY and DR. JACOB.

A salesman, aged 22, presented several marked depressions, the size of a split pea, on the cheeks. A milium body was noted at the edge of one depression and the patient said that each lesion began as a milium. No inflammatory reaction was noted at any time. The process was of one and one-half years' duration. Histologically, crater-like depression was noted, the base of which was below the level of the deeper layers of the surrounding epithelium. The surface was covered with cornifying epithelium. The cells in the involved epidermis were elongated and spindle shaped, lying perpendicular to the surface. The basal layer was composed of cells of the same character. A moderate lymphocytic infiltration was present, particularly under the edge of the lesion.

DISCUSSION

DR. ELLER: I believe that this is a case of dermatitis artefacta.

DR. CRAWFORD: Does the section show any signs of tricho-epithelioma?

DR. HIGHMAN: I saw the sections which are unique. One of the lesions shows a milium, which is probably exerting pressure on the surrounding tissue. The tissue around it is slightly infiltrated, fibroblasts are seen, and destruction and atrophy result in the pitting. I consider the lesion an atrophic process following the development of milia. I can give no definite name or classification to the lesion.

DR. VALADE: I think that there is a factitial element present.

DR. HOLLANDER: I suggest the diagnosis of morphea.

DR. GUY: The elongated cells extending all the way through the section make one think of basal epithelioma. The patient was seen a year ago and since that time the lesion has slowly enlarged. I believe that each lesion begins with a milium body, and that Dr. Highman's explanation is excellent. I suggest that they be removed by a plastic surgeon.

PEMPHIGUS VULGARIS (?). Presented by DR. HOLLANDER.

A woman, aged 20, was referred for treatment with blood transfusion on Aug. 30, 1928, by Dr. W. H. Guy. The condition on that day was as follows:

The finger-nails showed a definite change at the distal end, where the color was a brownish gray. There were a thickening and a tendency to enlargement, and the affected part of the nail was attached to the unaffected part by a series of ridges. The nails were highly arched laterally and softer than normal but not friable.

The skin showed extensive atrophy involving the entire upper extremities, more marked on the palmar and dorsal surfaces of the hands. About the elbows there was a marked reticulation, and when the skin was wrinkled the cigaret paper-like scarring was easily seen. Irregularly distributed here and there were little whitish nodules which were easily opened, and which contained a sebaceous material conforming in all respects to the appearance of milia.

The torso showed two types of scarring: anemic and hyperemic, much more to be noted on the back than anteriorly, and here again were great numbers of the previously described milia. About the buttocks there was a significant pigmentation. In one area there was an oval atrophy with a central depigmentation with a peripheral hyperpigmentation. The legs and feet showed a condition similar to the one described on the arms and hands.

On the face a healing bleb was noted, which was hemorrhagic. The eyelids were swollen and the palpebral conjunctiva inflamed. The presence of bullae here was reported but none was present at the time. There was a beginning atrophy at the end of the nose, otherwise the skin of the face appeared to be uninvolved except for a few red papules over the forehead.

An examination of the eye revealed that the patient had trachoma with spastic entropion. The onset was during November, 1927, as a bullous and hemorrhagic eruption. Tonsillectomy was performed in May at the Braddock Hospital, following a suggestion that the eruption was of toxic origin.

This patient was given six transfusions of whole blood of 500 cc. each, after which the condition improved and the patient was discharged from the hospital. At the time of presentation there was nothing but the atrophy of the skin, which resembled acrodermatitis chronica atrophicans.

PSORIASIS OSTRACEA IN A FULL BLOODED NEGRO. Presented by DR. AMSHEL.

A negro, aged 21, was seen for the first time on June 13, 1928, with a scaly eruption on the dorsal surfaces of the hands, extensor surfaces of the extremities and the trunk. The Wassermann reaction of the blood was negative. The case was originally presented with a diagnosis of psoriasis, but since the biopsy was negative for psoriasis, the diagnosis was not accepted. The scales were examined for fungi with negative results. After an interval of about six months the patient was seen at the clinic with a sore on the penis. Several dark-field examinations were negative for *Spirochaeta pallida* and the Wassermann reaction of the blood was negative. The eruption on the body was more pronounced, and a biopsy was taken from which a diagnosis of psoriasis was made. About the elbows, on the extensor surface of the forearms and on the thumbs, was an eruption consisting of hypertrophic, sharply marginated, scaly, rounded plaques varying in size from 0.5 to 4 cm. There were several large circinate patches of hyperpigmentation on the forearms surrounded by scaly papules varying from 0.3 to 1 cm. On the extensor surfaces of the legs and thighs were large areas of hyperpigmentation some with furfuraceous scaling. These areas were the remains of former lesions which subsided. No therapy had been instituted for the past week.

ACRODYNIA (ERYTHREDEMA). Presented by DR. CRAWFORD.

A boy, aged 6 years, three months before presentation developed photophobia and irritability with redness and swelling of the hands and feet and sausage-like edema of the fingers and toes. The eruption began with a fine miliarial rash accompanied by profuse perspiration. The photophobia disappeared after three

weeks, and the restlessness markedly improved after five weeks. During the past four weeks the child had had a persistent large papular eruption of the trunk, situated follicularly.

TUBERCULOSIS CUTIS (?) (NODULO-ULCERATIVE). Presented by DR. CRAWFORD.

Four years before presentation, a negro, aged 24, had small nodules on the back of his neck which broke down and discharged a small amount of yellow pus. After several months, nodules appeared on the trunk; at first they were shotlike; then they enlarged and broke down. Round or oval, dull red, papular lesions developed and enlarged peripherally from 1 to 4 cm. The surfaces of these lesions became eroded and presented a reddish uneven base with edges of a dull red, elevated and rounded appearance. A viscid seropurulent material was discharged from some of the lesions. Lesions were present on the face, neck, trunk, buttocks, arms and legs. Many of them had become confluent. On healing, they left slightly pigmented scars. The patient had periodic attacks of polyarthritis and tenosynovitis. Small superficial erosions in the larynx caused his voice to be husky. Coarse râles were heard at the apexes, and he frequently had night sweats. X-ray pictures of the chest did not reveal tuberculosis. In the axilla and groin large firm glands developed which were excised on four occasions. Culture showed acid-fast organisms and staphylococci.

PARAPSORIASIS GUTTATA. Presented by DR. GUY and DR. JACOB for DR. J. C. KERR.

A girl, aged 19, presented an eruption involving practically all of the covered parts of the body. The lesions were erythematous macules and papules, the size of a finger-nail with slight scaling. Subjective manifestations were absent. The condition was of four years' duration.

XANTHOMA DIABETICORUM. Presented by DR. SCHWARTZ and DR. BUSMAN.

A negro, aged 40, single, presented over the extensor surfaces of the arms and legs numerous yellowish nodules varying in size, from that of a pinhead to that of a split pea. There were also some on the palms and soles and a few widely scattered lesions. Lesions over the elbows were somewhat lichenified, flat and shiny. The condition was of three months' duration. Urinalysis was strongly positive for sugar.

DISCUSSION

DR. COMBES: This is an interesting case. The patient has typical xanthoma lesions in the sclera.

LICHEN PLANUS SCLEROSIS ET ATROPHICUS. Presented by DR. WERTHEIMER.

A woman, aged 58, was seen for the first time in July, 1922, with an eruption of three years' duration. This eruption was present on the flexor surfaces of the wrists, dorsal surfaces of the hands, the back of the neck in the hair line, the perianal region and in isolated spots on the neck comprising single and grouped, firm, ivory-colored, slightly elevated papules. The papules were shining and smooth, and minute dark, comedo-like plugs were observed on the surface. A mild ointment was prescribed, and about twenty-five intramuscular injections of mercuric salicylarsenate had been given. The condition improved somewhat with this treatment.

ADENOMA SEBACEUM GRANULOMA INGUINALE. Presented by DR. GOLDMANN.

A negress, aged 38, presented over the nose, cheeks and nasolabial folds multiple, soft nodules, varying in size from that of a split pea to that of a hazelnut. On the forehead there were darkly pigmented scars, the size of a split pea. This

condition had been present since early childhood. Involving the vulva and perianal region, the patient presented a serpiginous, punched-out ulceration, the borders of which were raised and grayish. This was of six years' duration. The patient had received approximately sixteen intravenous injections of arsphenamine and two of tartar emetic. The Wassermann reaction was negative; biopsy was refused. Scrapings from the ulceration were positive for Donovan bodies.

LYMPHANGIOMAS (AQUIRED). Presented by DR. SCHWARTZ and DR. BUSMAN.

A peddler, married, aged 42, presented a cauliflower-like mass involving the entire scrotum and right groin. The individual lesions were pinkish-white nodules, varying in size from that of a pinhead to that of an olive, filled with a milky white serum which exuded freely on pressure. There were also several transparent vesicles, varying in size from that of a pinhead to that of a pea, on the penile shaft and the right leg. There was an operative scar in both groins the result of a herniotomy in 1908. There was an appreciable elephantiasis of the right leg.

The condition started soon after the operation in 1908. There was continual drainage, and the leg soon began to enlarge. The cauliflower-like lesions developed about three years before presentation. The patient's general health was good. General examination, including a Wassermann test and urinalysis, gave negative results.

TERTIARY SYPHILIS (SYPHILITIC PERIOSTITIS OF THE RIGHT ORBIT). Presented by DR. HOLLANDER.

A man, aged 53, presented a tumor formation over the right inner canthus. The condition began in March, 1929, and since then had become progressively worse, causing proptosis with limitation of motion of the right eye to the nasal side, and a turning out to the temporal side. The vision of the right eye was almost nil except for light perception. The pupil was dilated and sluggish to light. The media were clear but there was some clouding of the disk edge with pallor to the temporal side. The left eye was also involved, but to a lesser degree, and showed no evidence of atrophy. Roentgenograms showed a diffuse increase in density over the frontal and ethmoidal sinuses and the left antrum. These areas and one in the region of the pineal body appeared calcified. The Wassermann and Kahn reactions of the blood were 4+.

GRANULOMA FUNGOIDES. Presented by DR. SCHWARTZ and DR. BUSMAN.

A woman, aged 39, single, presented over the face, upper part of the arms and trunk several annular, infiltrated, erythematous plaques, varying in size from that of a dime to that of a dollar. Also a diffuse thickening of the entire skin of the body with here and there some residual erythema and discoloration. There were no lesions of the mucous membranes. There was a generalized adenopathy.

Twelve years before presentation the condition started with a generalized itching of the skin, since which time the patient had never been entirely free. The condition gradually progressed until four years previous to presentation she presented a diffuse erythema with thickening of the entire integument. At times there had been slight improvement. She was always very sensitive to cold and suffered severely from generalized pruritus.

Blood counts and blood pressure were normal. The basal metabolism was decreased from 10 to 25 per cent. The functional test of the kidneys showed them to be normal. Septic tonsils were removed. Roentgenograms were taken of the teeth and the abscessed teeth extracted. The patient's condition was considered as a premycotic mycosis fungoides.

In June, 1928, she presented a few circular infiltrated plaques which disappeared when treated with roentgen ray. Since Jan. 1, 1929, the diffuse erythema and itching had subsided. At the time of presentation, she was comfortable, but presented more of the granuloma fungoides type of lesion.

LUPUS FOLLICULARIS DISSEMINATUS. Presented by DR. HOLLANDER.

A woman, aged 47, presented an erythematous papular eruption of the face, with scale-covered individual lesions and occasional pustules. The disease was apparently nonscar-producing and was of eleven months' standing. The patient presented no special symptoms except the cutaneous eruption. Study of the gastric contents revealed nothing of importance. Study of the blood and urine revealed only a somewhat high amount of creatinine, 2.08. Dentition was bad and recommendation for extraction of all the teeth had been made.

DISCUSSION

DR. BARNEY: This case is similar to one seen in Ann Arbor which Wile said looked like rosacea. Pustules, telangiectasia and associated gastric symptoms speak more for rosacea.

DR. MALONEY: I agree with Dr. Barney; I should expect more scarring in a case of lupus.

DR. NETHERTON: This is similar to the one seen at Ann Arbor and unless proved to be otherwise by biopsy, I should make a diagnosis of rosacea.

DR. HOLLANDER: I have changed my diagnosis twice. It is negative for rosacea from a gastric standpoint, the gastric juice being entirely normal. A few injections of a gold compound were followed by photophobia and were of no benefit.

TUBERCULOSIS OF THE HYPODERM TREATED WITH GOLD SODIUM THIOSULPHATE. Presented by DR. GUY and DR. JACOB.

A negress, aged 35, presented an erythematous scar covering both cheeks and the nose. A depressed scar, the size of a quarter, was present on the left side of the chin. These areas had previously been elevated, representing subcutaneous lesions. Biopsy showed tuberculosis. Several doses of roentgen ray, ½ unit, did not alter the lesions. Gold sodium thiosulphate in full 100 mg. doses was given at weekly intervals with good results. Thirty-five injections had been given. Several times the patient showed a swelling of the hands which disappeared when treatment was discontinued for a few weeks.

ICHTHYOSIFORM ERYTHRODERMA. Presented by DR. GUY and DR. JACOB.

A girl, aged 18, presented a generalized erythroderma with abundant scaling since birth. The hair and nails were normal. The condition was worse during the winter months. The general health was not affected. Histologically, a moderate hyperkeratosis was present, and an acanthosis with some edema both parenchymatous and interstitial in the rete. Considerable edema of the collagen was present. The capillaries were dilated and somewhat thickened, but practically no inflammatory infiltration was seen.

DERMATITIS HERPETIFORMIS. Presented by DR. HOLLANDER.

A woman, aged 24, presented a generalized eruption of twelve years' standing. The individual lesions were small vesicles and bullae which were distributed over the trunk and extremities. The face was free except for a few vesicular lesions about the lips which resembled herpes simplex. The larger bullae were tense and on an erythematous base. There was marked pigmentation in areas in which the disease had previously existed, and small areas of depigmentation which resembled scars.

KERATODERMA BLENORRHAGICUM. Presented by DR. GUY and DR. JACOB.

A man, aged 20, had acquired gonorrhea two and one-half years before presentation and had obtained apparent cure in two months. Two years later following an

alcoholic excess he noticed a slight discharge. After a few days he developed severe pain in the soles followed by arthritis of the hands, feet, jaw and cervical spine. About ten days later a papulovesicular and pustular eruption developed on the palms and soles. Some of the lesions underwent spontaneous resolution while others became thickened and keratotic. At the time of presentation, thick keratotic lesions involved the soles of both feet and the plantar aspect of several toes. At the base of the nail of the right small finger there was a single elevated, crusted, keratotic lesion, the size of a dime. The associated arthritis of the small articulations was apparent. There was an associated leukocytosis ranging from 10 to 16,000. The daily temperature varied from subnormal to 100 F. The gonorrheal complement fixation was positive. Orchitis of the left side, seminal vesiculitis and prostatitis were present.

PARAFFINOMA. Presented by DR. GOLDMANN.

A woman, aged 35, presented bilateral masses, the size of a walnut, in the cheeks. The masses were hard and were firmly attached to the underlying structures.

Fifteen years before presentation, while on the stage, the patient had paraffin injected into the cheeks.

MULTIPLE SARCOID OF BOECK. Presented by DR. SCHWARTZ, DR. BUSMAN and DR. WERTHEIMER.

A married man, aged 54, presented hundreds of raised intradermal nodules, varying in size from that of a pinhead to that of a dollar, over the forearms, the upper part of the arms and the face. The individual lesion was violaceous, raised and infiltrated and under diascopic pressure presented apple jelly-like nodules. The large, plaquelike lesions were made up of numerous small confluent nodules. There was some central atrophy and pigmentation in the older lesions.

From three to four years before presentation the first lesion developed at the site of a tattoo mark. Numerous sections have been removed with a pathologic diagnosis of sarcoid of Boeck.

The patient had had numerous injections of arsphenamine and prolonged treatment with solution of potassium arsenite. Local roentgen therapy had also been used repeatedly.

DISCUSSION

DR. CRAWFORD: Two years ago the diagnosis of sarcoid was considered along with that of disseminated tuberculosis. At present I favor the diagnosis of sarcoid.

DR. WERTHEIMER: Eighteen months ago a biopsy was made, and a diagnosis of sarcoid was verified by Dr. Satenstein.

ACUTE LUPUS ERYTHEMATOSUS. Presented by DR. GUY and DR. JACOB.

A merchant, aged 50, presented an eruption of five months' duration involving the face, scalp, chest and back. The onset was sudden. When first seen the lesions were erythematous papules with moderate scaling. Subjective symptoms were absent. Various applications did not improve the eruption which gradually flattened, assumed a dull dusky red color and became covered with tenacious scales which, particularly over the nose, dipped into the follicular orifices. The general health was not materially affected. General examination was negative except for infected teeth which were removed. A moderate leukocytosis was found. On account of the acute disseminated character, a gold compound was not used at first, but recently the patient had received 10, 20 and 50 mg. of gold sodium thiosulphate, with material improvement.

A CASE FOR DIAGNOSIS. Presented by DR. GUY and DR PHILLIPS.

A man, aged 34, presented a circular area of alopecia approximately 6 inches in diameter of four years' duration centering at the crown. A few small, crusted,

follicular pustules were noted at the border from time to time. The area of alopecia was atrophic. The pubic hair had also apparently been involved by the same process, the loss of hair being complete nine years prior to presentation.

DISCUSSION

DR. HIGHMAN: This is a difficult case to discuss. I do not agree with the previous pathologic diagnosis of lupus erythematosus. It has some of the appearance of lymphogranulomatosis, but alopecia of this sort is unknown in this disease. It does not conform to any type of alopecia with which I am familiar, and therefore I am unwilling to venture a diagnosis.

DR. HEMBOLD: This section was most peculiar. There is an intense subepithelial cell infiltration the nature of which I could not determine, but it was not inflammatory.

DR. TAUBER: I suggest the possibility of this being a traumatic alopecia

DR. BARNEY: I should suggest that a blood count and a section of a lymph node be made for comparison with the biopsy.

DR. GUY: When this case was first seen the pubic hair had been gone for nine years. There was never any inflammation and the hair fell out gradually and not as an extending patch. The histology suggested a lymphoblastomatous process and in spite of negative blood changes at present, future investigation may prove the essential nature of the condition.

CONGENITAL ALOPECIA. Presented by DR. GOLDMANN.

A girl, aged 16, presented a partial alopecia of the scalp, which had been present since birth. The same condition was present in a younger sister. The third sister was normal. The patient said that since she had reached puberty the condition had improved, and there had been an increase in the growth of hair. The Wassermann test and roentgen examination of the sella turcica gave negative results. The basal metabolism was +21. Examination of the hair under the microscope was negative for monilethrix.

DISCUSSION

DR. SCHEER: The appearance of the hair in this case and the presence of the same condition in her sister suggest to me the possibility of monilethrix.

DR. GOLDMANN: The hairs were examined and were not nodular.

DR. GUY: The history of early alopecia and slight regrowth at puberty suggests an endocrinous disturbance.

DR. GOLDMANN: Hair started to grow at puberty two years ago. The patient has a +21 basal metabolism.

GRANULOMA FUNGOIDES. Presented by DR. GUY and DR. JACOB.

A man, aged 71, presented lesions of three types scattered over the body. The condition was of four years' duration. On the left arm were three elevated, soft, granulomatous masses, the size of a palm, with sloping edges and some central destruction. Centering at the umbilicus was a deep, punched-out, gummatous type of ulceration, the size of a dollar. Similar lesions were present on the left flank and left buttock. Scattered irregularly over the covered parts of the body were numerous sharply marginated, slightly scaly, erythematous plaques varying in size from that of a nickel to twice that of a palm. One of those on the left buttock presented central ulceration. The patient had lost 40 pounds (18.1 Kg.). Itching had not been severe. The blood count revealed a moderate degree of secondary anemia with 2 per cent transitionals. Sections from the granulomas and gummatous type of lesions showed the usual granulomatous structure. The scaly plaques showed changes suggestive, but not diagnostic, of mycosis fungoides.

GRANULOMA FUNGOIDES. Presented by DR. HOLLANDER.

Miss M. B., aged 38, presented a generalized eruption of multiforme character on the hands, arms and greater portion of the face. There were large, infiltrated, brownish plaques which were extremely itchy. This patient had been attended since May 5, 1927. Under roentgen therapy some of the lesions disappeared, only to recur with increased intensity. Roentgen examination showed pyorrhea alveolaris with periapical infection, unerupted teeth in malposition and apparently infection in the frontal, ethmoidal and antral sinuses. A high creatinine content, 2.85, a moderately high sugar content, 141, and a trace of albumin in the urine were found.

ARGYRIA. Presented by DR. BEINHAUER.

A man, aged 46, presented a discoloration of the face, neck, arms, hands and body, which had been present for the past five years. The patient had been under treatment until a recent operation for gastric ulcer and had been taking silver nitrate by mouth for the past seven years. Approximately 472 grains (26.68 Gm.) of silver nitrate had been taken internally. The skin of the entire body presented a modified color change varying from a light slate over the covered parts to an extreme gun metal or bronzing over the face, neck and flexures of the arms. The mucous membrane presented a mottling not unlike a lead pigmentation. The hair was definitely henna in shade. The patient had received sodium thiosulphate by mouth and intravenously for one year, with a marked decrease in the pigmentation.

EPIDERMOLYSIS BULLOSA HEREDITARIA. Presented by DR. WERTHEIMER.

A girl, aged 7, was first seen in 1925, with an eruption that had been present since birth. On and between all the fingers were numerous vesicles and denuded areas. On the palms were broken vesicles and large areas of denudation. Several erythematous, vesicular and pustular areas, varying in size from that of a pea to that of a dollar, which were secondarily infected, were seen on the arms, elbows, knees and lower extremities. In these patches were groups of small miliary bodies, the size of a pinhead. Both thumb nails were markedly thickened. Her sister had a similar condition.

EPIDERMOLYSIS BULLOSA HEREDITARIA. Presented by DR. WERTHEIMER.

A girl, aged 4, was first seen in May, 1926. On the extensor surfaces of the fingers and toes, and between them, were whitish areas, the size of a small pea, made up of numerous vesicles, varying in size from that of a pinpoint to that of a pea. A few small bullae were present at that time. She was seen again in 1929, with little change in the picture. The child had a low mentality. A sister had the same condition.

EPIDERMOLYSIS BULLOSA HEREDITARIA. Presented by DR. BEINHAUER.

A boy, aged 4 years, at the time of the first examination, presented an extensive, foul, bullous, impetiginous eruption involving the face, neck, hands, lower part of the abdomen, buttocks, legs and feet, which had been present for four months. At the age of 7 months the parents noted that trauma produced a bullous lesion which became secondarily infected and persisted for from two to four months. At the age of 18 months, a generalized loss of hair was noted, at which time infection of the ears and eyes ensued. For the past three years, the patient had been bedridden most of the time. Examination revealed an emaciated child afflicted with marked photophobia, with extremities flexed on the body and chin flexed on the chest. The head was hydrocephalic with total absence of hair. A marked nasal and conjunctival discharge was present. The liver and spleen were palpable. The reflexes were exaggerated. The Wassermann reaction, blood picture and urinalysis were negative.

DISCUSSION

DR. GUY: I think that a congenital ectodermal defect in this case is associated with the epidermolysis bullosa.

LUPUS ERYTHEMATOSUS. Presented by DR. GUY and DR. JACOB.

A woman, aged 38, when first seen in 1925, presented a butterfly type of eruption on the nose and cheeks. Gold sodium thiosulphate was administered at weekly intervals for twenty weeks, when she suddenly developed a generalized eruption. Doses of sodium thiosulphate twice weekly cleared up the generalized eruption in approximately two months. Then, beginning with 5 mg., a gold compound was again administered in ascending dosage without reaction and with improvement in the original lesion, remnants of which were present at the time of presentation.

ADDITIONAL CASES.

Twenty-four additional cases were presented and discussed.

ST. LOUIS DERMATOLOGICAL SOCIETY

NORMAN TOBIAS, M.D., *Secretary*

Regular Meeting, Nov. 13, 1929

ROBERT H. DAVIS, M.D., *President*

A CASE FOR DIAGNOSIS. Presented by DR. GEORGE D. REEVES.

L. O., a woman, aged 24, presented an eruption on the palms and soles which had started about two weeks before examination, as small blisters on the soles. The lesions were small erythematous papules, hard and shotty to touch. Among these were a few deep-seated vesicles, which, when opened, exuded a clear fluid. The older lesions were hard, darkly pigmented macules. The remainder of the body was free from any dermatitis. The patient gave no history of primary lesion. The Wassermann reaction of the blood was 4 plus.

DISCUSSION

DR. GRINDON: This case is an example of what the French call, syphilide cornèe. They are syphilitic papules with a distinct border of infiltration and a scaling center.

DR. CONRAD: I agree with Dr. Grindon that the case is one of syphilis. I suggest that an examination be made to discover the presence of a primary lesion if possible.

DR. TOBIAS: The eruption is typically a syphilitic one. It belongs to the group of late manifestations of early syphilis.

VITILIGO. Presented by DR. GEORGE D. REEVES.

E. K., a woman, aged 30, was presented as representative of five patients with vitiligo whom we had treated with gold sodium thiosulphate. Our patients received from three to eight injections of 1½ grains. (0.09 Gm.) of gold sodium thiosulphate with no noticeable result.

DISCUSSION

DR. GRINDON: Recently a pharmacologist told me that he saw improvement in vitiligo when eau de cologne was rubbed on the patches before the ultraviolet light was used. It is possible that the fluorescence of the oils in the cologne modified the violet rays.

DR. LANE: This case is one of three in the clinic in which treatment for vitiligo with gold sodium thiosulphate has been used. So far we cannot share

the optimism of other workers who have had success with this treatment, as none of our patients have shown any improvement.

DR. GRINDON: In this country, the terms leukoderma and vitiligo are generally used interchangeably. The Germans mean by leukoderma a loss of pigment secondary to some inflammation, as occasionally seen in psoriasis and oftener in neurodermatitis. They restrict the term vitiligo to a purely pigmentary disturbance. Some of the latter class are syphilitic.

LEUKOPLAKIA. Presented by DR. GEORGE D. REEVES.

E. L. J., a man, aged 57, had noticed white spots in his mouth for four or five years preceding examination. They caused him no pain. They were not progressive, nor did they seem to disappear. There was an irregularly thickened whitish patch covering the hard palate and upper gums. The tissues that were not covered were angry red and inflammatory. The patch seemed to be adherent but it could not be removed.

DISCUSSION

DR. TOBIAS: I have no doubt that this is a case of leukoplakia. As to treatment, I do not think that I would use any treatment in this case, because often we become too energetic in our treatment and later as a result, have a carcinoma to deal with. I believe that prophylaxis and prevention are indicated. The patient should take care of the teeth, see that bridgework or plates fit properly, stop the use of tobacco and use a mouth wash. Radium or the cautery should be used if any signs of inflammation occur. I would advise no treatment beyond prophylaxis in this case.

DR. GRINDON: I agree with Dr. Tobias. I use a 2 per cent solution of sodium salicylate for treatment in my cases. It can be made up in large quantities and kept at the patient's home and office, with instructions to use it the first thing in the morning, the last thing at night, after meals, and whenever he thinks of it. Tobacco should not be used, but a patient will not get well just by ceasing to use tobacco. The more radical measures tend to make things worse. If radium is used, it should be only by some one who is a master in its use. All leukoplakias are not alike. On the palate one sometimes sees a sheet of leukoplakia with the appearance of an egg shell membrane that has been laid over the surface and the border trimmed off sharply. The edge of the thickened epithelium perhaps turns over. One sees a different form on the tongue and lips. On the tongue the thickening gives a rugous appearance, like the folds on the scrotum.

DR. BROCKELMANN: In the early stages of leukoplakia, I find most important to be observation and prevention of any irritation caused through rough edged teeth, the use of tobacco, highly spiced food, etc. Local applications of tincture of myrrh may often prove helpful in these cases. In advanced cases, the majority of writers seem to prefer surgical measures rather than treatment with radium.

DR. TOOMEY: I do not think of anything that could be done palliatively other than the measures which Dr. Grindon has suggested. I believe a patient with leukoplakia should be kept under monthly observation, and that if the leukoplakia shows any tendency to extend under simple treatment, it should be dealt with radically by plastic surgical methods or the actual cautery. According to my experience, radium or the roentgen rays do not give permanent, definite results in a sufficiently large proportion of cases, and may, on the other hand, make matters worse by causing the leukoplakia to undergo a highly malignant degeneration. For this particular patient I would suggest no radical treatment at present, but I feel that he will ultimately require electrocoagulation or a complete curetting out of the lesion under a general anesthetic.

DR. CONRAD: I have seen patients aided by treatment with the electric spark or electrotherm. These lesions were on the lips, and were of the thickened kind. They cleared up under fulguration.

DR. GRINDON: Are they still under observation?

DR. CONRAD: I have some under observation for one year after treatment.

DR. DAVIS: The danger in the use of the electrotherm or of superficial surgical measures is that a carcinoma might result.

DR. TOOMEY: I meant radical surgical measures with the actual cautery, or the knife followed by skin graft. I have seen two cases of lesions of the lip apparently do well under fulguration, but as the latter is usually carried out, it is inadequate, a complete electrocoagulation of all the leukoplakic tissues should be obtained.

DR. DAVIS: The condition is like a sleeping dog; there is no harm in letting it alone.

DR. LANE: In leukoplakias showing evidence of malignant change or in which this change is suspected, radical excision followed by skin graft seems to offer the best chance of permanent cure.

A CASE FOR DIAGNOSIS. Presented by DR. GEORGE D. REEVES.

H. J. V., a man, aged 60, presented himself with a large punched-out ulcer involving the soft palate and anterior pharyngeal wall, and which had endured for two months. He did not complain of much pain nor was he inconvenienced by it. The ulcer seemed to be spreading. The Wassermann reaction of the blood was negative. The patient was put on regular antisyphilitic treatment and after about two weeks another Wassermann test of the blood was made, which gave negative results. A smear from the throat gave positive results following an examination for Vincent's sign. The antisyphilitic treatment was continued, but the throat has, however, continued to become worse. No diagnosis was made. Biopsy of the throat and roentgenograms of the chest were requested, and the patient is to be presented at a later date.

DISCUSSION

DR. TOBIAS: It is difficult to make a diagnosis based on inspection alone, because there are certain shortcomings in the laboratory work, but from the nature of the inflammatory reaction I think it is hardly a carcinoma or syphilitic lesion. My tentative diagnosis is tuberculosis of the soft palate and uvula.

DR. LANE: There is a positive Vincent's sign.

DR. CONRAD: I do not think that the condition is syphilitic. The patient had had enough antisyphilitic treatment to clear this up if it were.

DR. TOOMEY: I am confident that the lesion is carcinomatous. The hard, clean, glistening, multiple mammilliform appearance of the upper pole of the left tonsil looks definitely carcinomatous to me. Besides, the lymphatic extensions are not so sclerous in tuberculosis.

DR. DAVIS: The lesion is probably a carcinoma or another possibility is tuberculosis. I do not think that it is syphilis. I do not think one could make a definite diagnosis without making a section. I believe it is a carcinomatous lesion, but that is just an impression.

DERMATITIS MEDICAMENTOSUM (BROMIDE). Presented by DR. GEORGE D. REEVES.

M. B., a woman, aged 48, was given some capsules for rheumatism by a physician about two months before presentation. She took these and about two or three weeks later, an eruption began to appear on her skin. She then presented a generalized maculopapular eruption over the face, chest, back and lower limbs. The papules were about as large as a pea and were shotty, very red and itchy. Most of the lesions had disappeared, leaving darkened pigmented areas. There existed then two darkened areas on the lateral aspect of the right leg;

the upper about 2 by 3 inches (5 by 7.6 cm.); the lower about 1 by 2 inches (2.5 by 5 cm.). These, she said, started just like the others, but continued to get worse. The areas had become denuded of epithelium, leaving a very red, pitted, granulating surface covered with a thin white pus. The borders were hemorrhagic, forming a purple band about 1 cm. wide between the ulcer and normal skin. The ulcers were very painful. The examination of the urine gave negative results; the blood count was normal, and the Wassermann reaction of the blood was negative.

DISCUSSION

DR. GREINER: I thought the condition either a bromide or an iodide eruption.

DR. TOOMEY: I thought of a blastomycosis, but the borders are too clean, regular and smooth for this. It looks like an iodide rash, perhaps helped along with phenobarbital from the capsules. I think it would be interesting to get more data on the combinations of drugs; what effect phenobarbital would have on a given quantity of iodide, etc. If it were a coccidioidal granuloma, the lesions on the elbow would not have healed over under the treatment she has had.

DR. DAVIS: I believe that it is a bromide or iodide rash. The patient might be helped by arsenic therapy in addition to the regular treatment of light, etc.

DETROIT DERMATOLOGICAL SOCIETY

H. J. PARKHURST, M.D., *Reporter*

Regular Meeting, Nov. 19, 1929

ARTHUR E. SCHILLER, M.D., *Presiding*

URTICARIA PIGMENTOSA. Presented by DR. SCHILLER and DR. SCHLEGELMILCH.

R. H., a boy, aged 4 years, had had a persistent eruption of brown macules on the trunk and extremities for a year and a half. When rubbed, the macules became wheals.

DISCUSSION

DRS. VAN RHEE, KEIM and JAMIESON agreed with the diagnosis as presented.

CHRONIC PAPULAR URTICARIA. Presented by DR. SCHILLER and DR. SCHLEGELMILCH.

S. N., a girl, aged 3 years, was said to have had an eruption since early infancy, the condition having improved in winter and grown worse in summer. On the arms and legs, especially on the extensor aspects, were many small papules, most of which were excoriated and crusted. Dermographism had been demonstrable at times. Under a restricted diet there had been no improvement.

DISCUSSION

DR. JAMES: The matter of treatment presents a problem in such cases. Lately I found a case in which the patient was sensitized to milk, but after that had been removed from the diet, the eruption recurred.

DR. PARKHURST: In the New York hospitals such cases are common, and malnutrition is considered an etiologic factor. Improvement of the nutrition and general hygiene is often helpful in effecting a cure.

DR. JAMIESON: In the *Urologic and Cutaneous Review* some one has recommended the use of spleen extract in chronic urticaria. I tried it recently, with prompt improvement, in a stubborn case of four years' duration. Last spring,

on the advice of an internist, roentgen irradiation of the spleen had been done with no apparent effect on the urticaria.

KERATOSIS PALMARIS ET PLANTARIS (?). Presented by DR. SCHILLER and DR. SCHLEGELMILCH.

E. C., a woman, aged 41, had first been seen three years previously, with a positive Wassermann reaction. After the administration of a total of 1.8 Gm. of neoarsphenamine, arsenical treatment had been discontinued because of a marked skin reaction. Following this, a total of 19 cc. of bismuth and 12 cc. of mercury salicylate had been given intramuscularly, and the Wassermann reaction had become persistently negative. No treatment had been given in 1928 or 1929, and on July 2, 1929, the Wassermann reaction was still negative. There were pronounced keratotic lesions on both soles and a recurrent keratotic patch on the right palm. No treatment had been instituted.

DISCUSSION

DR. SHAFFER: In this case it is hard to make a definite diagnosis without observation. It looks like a syphilid, but the short duration, sharp limitation and recurrence speak for dermatophytosis. It is not keratosis palmaris et plantaris nor arsenical keratoses and is not psoriasis nor lichen planus.

DR. PARKHURST: The infiltration, dryness and gyrate arrangement of the lesions, and the asymmetry of the involvement of the hand favor a diagnosis of syphilis rather than dermatophytosis.

DR. VAN RHEE: I consider the lesions syphilitic.

DR. KEIM: I feel that the eruption is syphilitic. We must not be influenced by the negative laboratory results.

EROSIO INTERDIGITALIS BLASTOMYCETICA. Presented by DR. SCHILLER and DR. SCHLEGELMILCH.

Mrs. Y. D., a Russian Jewess, had first noticed erosions between the third and fourth fingers of the left hand thirty years previously. The condition had persisted and extended, involving the webs between all of the fingers of both hands. The areas were moist and grayish white, with an inflammatory base. Many yeast cells and mycelia were present in cultures, but no spores. No mycelia or spores were found in scrapings.

DISCUSSION

DR. KEIM: I have never seen one so resistant to treatment and so extensive.

PERFORATING ULCERS OF THE FEET. Presented by DR. SCHILLER and DR. SCHLEGELMILCH.

R. A., a negro, aged 42, presented a painless ulcer, about 3 cm. deep, with cornified border, on each sole in the region of the first metatarsophalangeal joint. The surrounding tissues were boggy and edematous. There were smaller ulcers on the plantar aspects of both great toes. The discharge was foul and seropurulent. Both ulcers had appeared in callouses: the one on the right foot two years and that on the left four months before the time of presentation. The patient had had a chancre in 1916, followed by treatment at intervals. The Wassermann reaction of the blood was negative, while the reactions on the spinal fluid were strongly positive. The neurologic signs of tabes were present; there was optic atrophy. Roentgenologic studies showed an advanced destructive process involving several metatarsophalangeal joints and adjacent bones.

DISCUSSION

DR. SHAFFER: This case is interesting because of the extensive involvement and because the patient is a negro. Treatment is not likely to help.

DR. SCHILLER: How common are such cases?

DR. JAMIESON: During a period of fifteen years at Harper Hospital we have seen one case.

DR. KEIM: They were not uncommon at Ann Arbor: about six or eight a year, I should estimate.

A CASE FOR DIAGNOSIS. Presented by DR. SCHILLER and DR. SCHLEGELMILCH.

R. J., a man, aged 26, had had ulcers on the right leg for nineteen years. He disclaimed knowledge concerning their origin. There had been sharp, shooting pains and muscle cramps in the leg for the last two years, with tingling sensations. The leg and ankle swelled in the afternoon, and the leg was usually purple. There was a tender, dusky red, serpiginous ulcer with sharp, indurated margins and a smooth center showing two points of suppuration. The ulcer was over the tibia in the middle third of the leg, with several varicose veins visible above it. The patient had had a penile sore in 1926, but the Wassermann reaction was negative. Roentgenograms of the tibia, fibula and ankle of the affected leg showed cortical and periosteal changes highly suggestive of syphilitic processes.

DISCUSSION

DR. JAMIESON: Has a therapeutic test for syphilis been tried? If there was no response to it, I should consider the condition an artefact. It began too early to be varicose.

DR. PARKHURST: There are varicose veins in the leg and bogginess around the ulcer, but the angular outline of the lesion favors a diagnosis of dermatitis factitia.

DR. KEIM: It may be of trophic origin, due to vascular injury.

A CASE FOR DIAGNOSIS. Presented by DR. SCHILLER and DR. SCHLEGELMILCH.

B. F., a colored schoolgirl, aged 15, stated that two months previously she had first noticed a pruritic pustular eruption on the wrists, elbows and legs. This persisted, with crusting, and a papular and vesicular eruption, with lesions varying in size from that of a pinhead to that of a pea, extended over the ankles, knees, popliteal spaces, groins and breasts. The Pirquet reaction was negative with bovine and human organisms, and the Wassermann reaction was negative. There had been considerable improvement under treatment with potassium iodide.

DISCUSSION

DR. JAMIESON: At present the eruption resembles an involuting secondary syphilid, but I can make no definite diagnosis.

SYCOSIS VULGARIS; RADIODERMATITIS; SEBORRHEIC DERMATITIS. Presented by DR. VAN RHEE.

W. B., a man, aged 24, a laborer, presented a highly inflammatory eruption of follicular pustules on the forehead, eyebrows, cheeks, upper lip and neck, together with ulceration of the eyelids and ectropion, and fissuring of the oral commissures. Both cheeks showed areas of atrophy and hair loss. The eruption had first appeared on the eyelids ten years previously, spreading slowly, and involving the cheeks and chin three years before presentation. Various local applications had been used, and four roentgen treatments had been administered two years before presentation. Autogenous vaccines, moist dressings and ultraviolet therapy were being used.

DISCUSSION

DR. SHAFFER: Is this not lupoid sycosis (ulerythema ophryogenes)? I have used ionization with a compound solution of iodine in one case, apparently with good results.

DR. PARKHURST: In Cleveland Drs. Cole and Driver are getting good results with solid carbon dioxide in an old case of sycosis, resistant to other treatment.

DR. VAN RHEE: The atrophic areas seem chiefly due to roentgen exposures.

A CASE FOR DIAGNOSIS. Presented by DR. VALADE.

E. H., a man, had first noticed a vesicular eruption between the toes and on the dorsum of the right foot, in a dollar-sized patch, in September, 1928. This had responded for a time to the usual treatment for dermatophytosis. Subsequently scattered coin-sized groups of deep vesicles had appeared on the legs, thighs and upper extremities, with intense itching. Mycelia were found in scales from the lesions on the foot.

DISCUSSION

DR. JAMIESON: I have often sought the organism in such cases. They look like dermatophytosis.

DR. SHAFFER: We are all seeing cases diagnosed as eczematoid ringworm of the hands and feet, on which no fungus are shown. Some of the New York dermatologists feel that this is a trichophytid, with a small focus of original infection. This focus, which may be small, must be found and eradicated.

Book Reviews

HISTOLOGISCHE TECHNIK DER HAUT. By HOEPKE. Price, 18 marks. Pp. 208, with 64 illustrations, some of them in color. Berlin: Julius Springer, 1930.

This monograph, taken from Professor Hoepke's "Handbook of Skin and Venereal Diseases," covers in the most comprehensive and detailed way the technic of histopathology of the skin. It is a laboratory working guide to the subject of great value. The illustrations of both apparatus and methods of procedure are numerous and instructive. The histologic illustrations are few, which is not a criticism on a book devoted to technic, but these few are mostly in colors and are excellent. It is a valuable book for dermatologists.

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Directory of Dermatologic Societies *

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

William H. Guy, Chairman, Jenkins Arcade, Pittsburgh.
Francis E. Senear, Secretary, 55 E. Washington St., Chicago.
Place: Detroit. Time: June 23-27, 1930.

American Dermatological Association

Udo J. Wile, President, University Hospital, Ann Arbor, Mich.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.
Place: Cleveland. Time: June 19-21, 1930.

British Association of Dermatology and Syphilology (Canadian Branch)

Gustave Archambault, President, 544 East Sherbrooke, St., Montreal.
Albéric Marin, Secretary, 544 East Sherbrooke St., Montreal.
Place: Montreal. Time: June, 1930.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore and Washington Dermatological Society

Frank J. Eichenlaub, President, 1835 I St., N. W., Washington, D. C.
Leon Ginsburg, Secretary, 1800 N. Charles St., Baltimore.

Iowa and Western Illinois Dermatological Association

Robert E. Jameson, President, 1015 First National Bank Bldg., Davenport, Iowa.
A. T. Leipold, Secretary, 1419½ 5th Ave., Moline, Ill.

New England Dermatological Society

Walter T. Garfield, President, 19 Bay State Rd., Boston.
Rudolph Jacoby, Secretary, 270 Commonwealth Ave., Boston.

Southern Medical Association, Section on Dermatology

Jeffrey C. Michael, Chairman, 1017 Medical Arts Bldg., Houston, Texas.
Emmet R. Hall, Secretary, Exchange Bldg., Memphis, Tenn.

STATE DERMATOLOGIC SOCIETIES

Louisiana Dermatological Society

M. T. Van Studdiford, Pere Marquette Bldg., New Orleans.
Thomas A. Maxwell, Secretary-Treasurer, 1119 Union Indemnity Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Walter J. Highman, Chairman, 853 7th Ave., New York.
Albert R. McFarland, Secretary, 348 University Ave., Rochester.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON DERMATOLOGY

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Sigmund S. Greenbaum, Secretary, 1714 Pine St., Philadelphia.

MINNESOTA DERMATOLOGICAL SOCIETY

Edward C. Gager, President, 350 St. Peter St., St. Paul.
D. D. Turnacliff, Secretary, Yeates Bldg., Minneapolis.

OKLAHOMA DERMATOLOGICAL ASSOCIATION

M. M. Roland, President, 117 N. Broadway, Oklahoma City.
W. A. Showman, Secretary, 108 W. 6th St., Tulsa.

LOCAL DERMATOLOGIC SOCIETIES

ATLANTA DERMATOLOGICAL SOCIETY

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H. S. Alden, Secretary, Medical Arts Bldg., Atlanta, Ga.

BRONX DERMATOLOGICAL SOCIETY

Charles A. Greenhouse, Chairman, 1401 Grand Concourse, Bronx, New York.
Ralph Breakstone, Secretary-Treasurer, 783 Beck St., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

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A. M. Persky, Secretary, 1750 Ocean Pkwy., Brooklyn.

CHICAGO DERMATOLOGICAL SOCIETY

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E. A. Oliver, Secretary, 55 E. Washington St., Chicago.

CINCINNATI DERMATOLOGICAL SOCIETY

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R. R. Du Casse, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

CLEVELAND DERMATOLOGICAL SOCIETY

Clyde L. Cummer, President, 2417 Prospect Ave., Cleveland.
Robert E. Barney, Secretary, Osborn Bldg., Cleveland.

DETROIT DERMATOLOGICAL SOCIETY

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William G. Schlegelmilch, Secretary-Treasurer, 9203 Grand River, Detroit.

LOS ANGELES COUNTY MEDICAL ASSOCIATION, DERMATOLOGIC SECTION

George F. Koetter, Chairman, 1136 W. 6th St., Los Angeles.
H. Sutherland-Campbell, Secretary, 1936 Wilshire Blvd., Los Angeles.

MANHATTAN DERMATOLOGICAL SOCIETY

David L. Satenstein, Chairman, 57 W. 57th St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

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NEW YORK DERMATOLOGICAL SOCIETY

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PHILADELPHIA DERMATOLOGICAL SOCIETY

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Carroll S. Wright, Secretary, 1402 Spruce St., Philadelphia.

PITTSBURGH DERMATOLOGICAL SOCIETY

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Louis Willard, Secretary, 328 Jenkins Bldg., Pittsburgh.

ST. LOUIS DERMATOLOGICAL SOCIETY

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Norman Tobias, Secretary, Missouri Bldg., St. Louis.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Thomas Clarke, Madison-Lake Apts., Oakland, Calif.
H. J. Templeton, Secretary, 3115 Webster St., Oakland, Calif.